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THE SURGICAL FOLLOW-UP DEPARTMENT OF THE NEW YORK HOSPITAL

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IT IS not the dexterity with which he performs an operation nor the number of operations he can do in a day that comprises the surgeon's summum bonum; these things are ephemeral. But rather it is the ultimate good done the patient and the final result of the surgeon's judgment and skill. This can rarely be estimated by how well the patient recovers from the anesthesia, nor his postoperative course in the hospital, nor even how he is doing the first few weeks after he leaves it. It must usually be the summation of the patient's gains, and losses if there be such, after a suitable period of time considered in terms of months or years. Surgeons on the whole admit this and many earnestly strive as individuals, or through their clinics and hospitals, to carry on an efficient follow-up service. Others, through lack of interest, time or finances neglect this important field.

It is my purpose to present in detail the methods employed by the Surgical Department of the New York Hospital in following the patients after they leave the hospital.* Such methods, to efficiently produce satisfactory results, require careful organization, a certain amount of funds and a sustained interest by members of the surgical staff. It is realized that a method that is ideal in one hospital might be entirely inadequate in another, but it is hoped that by comparison this résumé may be of value to those who have had difficulties with their follow-up work and stimulate those who are neglecting it.

The Surgical Department of the New York Hospital serves as the teaching unit for the Cornell University Medical College, and consists of a combined full time and part time attending staff and a house staff working under the resident system. The wards accommodate about 180 beds for all types of general surgery, orthopedics and urology, and admit, on the average, 2,750 patients a year. The hospital employs the "central unit record system" with an individual chart for the case records of each patient. This chart includes in chronologic order all of the patient's inpatient and outpatient rec-

* This report concerns the New York Hospital since its reorganization and occupancy of its new building, September 1, 1932. Dr. Charles L. Gibson described the Surgical Follow-up Department effectively used in the old hospital, in three articles appearing in the ANNALS OF SURGERY for the years 1916, 1919 and 1928. Submitted for publication January 21, 1937.

ords. Incidentally, the Standard Classified Nomenclature is used for indexing disease, and an operation index has been perfected as well. These indices are kept by the hospital Record Department.

The purpose of the Surgical Follow-up Department is to maintain a system whereby examinations can be periodically made and recorded on surgical patients after they leave the hospital until their conditions can safely be considered cured, at a standstill, or fatal.

This work is under the direction of the Surgical Department and under the supervision of one member of the staff who assumes responsibility for overseeing it. Two secretaries are employed who maintain the files and do the secretarial work necessary to contacting patients. Volunteer workers can be used to advantage here, but there must be at least one capable and responsible secretary. The Social Service Department investigates all cases that the secretary is unable to contact.

The equipment necessary consists of filing cabinets, secretaries' desks, typewriters and other stenographic supplies. The files consist of (1) a "name file," and (2) a "date file."

The first file, or "name file," includes a "name card" (size 3x5 inches) for each patient to be followed after he is discharged from the surgical ward. (A new card is made out for each readmission and clipped to the original.) The card is indexed under the patient's name and possesses the following information:

Name	Age	Hist. No.
Address		Ward
Date of Admission		Date of Discharge
Diagnosis		
Operation		
Operator		
Result at Discharge		

On the reverse side of the card, brief notations are entered at intervals after the patient's discharge from the hospital, which give at a glance what efforts have been made to contact him and, in a word, what his condition was when last examined. A few examples of notes which might appear on this side of the card are as follows:

Date—6 mos. p.o. result good.
Date—No response to first request.
Date—Letter returned "not found."
Date—Letters to relatives and referring M.D.
Date—Social Service reports patient died.
Date—Report of death and autopsy from attending M.D.

Corresponding to each such entry on this card will be a similar, or if necessary, a more complete one on the patient's hospital chart, for it is meant that the hospital chart shall carry the complete record and that these cards serve only as convenient information for the secretarial work.

The second file or "date file" is a familiar system for grouping patients with the same clinic appointment dates. An example of its function is as follows: If a patient leaves the hospital September 1, 1936, his next visit for a check-up may be six months hence, or March 1, 1937. The "date card" headed by the patient's name is filed together with all other cards of patients to be seen on this date. As new appointments are made for the patient, the card will be moved up to the desired date.

The mechanism for establishing the name and date files would vary in different institutions depending on their respective organizations. In this hospital, the Record Department stencils a series of cards when a patient is admitted (using name, address, history number, ward and date of admission) and these cards are distributed to the accounting office, post office, information desk, head nurse and floor clerk. The floor clerk keeps two of these stenciled cards until the patient is discharged. When he is discharged, the house officer writes a summary, makes the final diagnosis and indicates when the first visit to the Follow-up Clinic shall be. The patient's chart with this information automatically passes through the hands of the floor clerk, and it is a simple matter for her to fill in the needed information on the two cards she has been holding. On one card is added the diagnosis, operation, operator, *etc.*, and this becomes the "name card." On the other card is written the date designated for the first follow-up appointment, and this card becomes the "date card." The two are then sent to the follow-up secretary for filing.

There will, of course, be cases from which there is nothing to be gained by subsequent examinations and others which, for one reason or another, are not suitable for surgical follow-up purposes. A list of some of these would include cases with (a) nonsurgical diseases, (b) "no disease" or "no diagnosis," (c) "discharged against advice" and (d) minor surgical ailments. The stenciled cards of these patients whom the house officer indicates need not be followed are destroyed by the floor clerk. This means that the Follow-up Department will not be a complete registry of surgical cases; but that is not its purpose. Registries should be available elsewhere.

The Follow-up Clinic at which the patients are examined when they return for their periodic check-up is held in the Outpatient Department of the hospital on Sunday from 9:30 to 12 A.M. On Sundays a majority of patients find it more convenient to attend such a clinic than on week days, there is no conflict with the regular work of the Outpatient Department, and physicians are less apt to be occupied with regular duties. About 35 of these clinics are held during a year, there being none on or near holidays or during the midsummer weeks. An average of 110 patients attend each week and a sufficient number of doctors, nurses and attendants are present to see that patients are cared for efficiently. The usual numbers are 12 doctors, two nurses, two attendants, and two secretaries. Each patient's chart, having been requisitioned the previous day from the Record Department, is on hand and a page stamped with the words "Surgical Follow-up" and the date. Be-

neath this, the examiner will write a brief but inclusive note, using the following form as a guide:

(*a*) History:
How was the recovery from operation?
How does the patient feel now?
Is he relieved of symptoms for which he came to the hospital; are they improved, the same or worse?
Has he resumed work in part or wholly?
Has he any new complaints? Are they associated with the original malady?

(*b*) Examination:
Description of pertinent physical findings.
Description of wound, function of parts, *etc.*

(*c*) Advice:
Regarding activity, diet, medication, *etc.*

(*d*) Recommendations:
Further examinations as roentgenologic, basal metabolism.
Refer to regular Outpatient Department for further study or care.
Refer for readmission to hospital.

(*e*) Statement as to interpretation of RESULT of operation (exclusive of any complaints or conditions unrelated to the operation).
(1) Good (excellent, satisfactory, relieved, *etc.*)
(2) Fair (improved, partially relieved, *etc.*)
(3) Poor (unimproved, worse, complications, *etc.*)

(*f*) Case closed or date set for next appointment to Follow-up Clinic.

(*g*) Unoperated cases should have an intelligent note regarding the condition of the patient's original malady, *i.e.*, subsidence, persistence, progress, *etc.*

The secretary will copy the RESULT on the back of the patient's "name card" and set the "date card" ahead to the date of the next appointment or destroy it if the case is closed. She will arrange for the various appointments which may have been recommended for special examinations, or to the Outpatient or Inpatient Departments.

The length of time for following cases and the intervals between visits are given below for a number of the usual surgical conditions and these suggest comparable intervals for conditions not listed. It is expected that these periods can be varied in any way that seems advisable for the particular case, but there must be some uniformity, and it is to be borne in mind that a case is to be followed as long as there is reasonable chance of a change in the condition. If a patient needs to be observed more frequently than at four monthly intervals, he should be referred to an Outpatient Clinic. This applies also to the few visits which may be necessary for dressings and observations immediately after discharge from the hospital (Table I).

Obviously, if someone wishes to make a special study of gastric operations for ulcer after ten years (the regular period for following these being only five years), he has only to go to the index of operations in the Record Department of the hospital, list his cases and have them notified by the secretary of the Follow-up Department.

Several days before time for the patient to appear at the Sunday Follow-up Clinic, the appended, 6x3½ inch, orange colored card is sent him in an unsealed envelope:

NEW YORK HOSPITAL

Name.....History No.....
Will you please come to the Surgical Follow-up Clinic, 5th Floor, K Bldg., on Sunday morning.....at.....o'clock
so that we may note your progress since you left the Hospital?

This service is given free of charge.

Bring this card with you and use the entrance at 516 East 70th Street. If you cannot come, call REgent 4-6000 Extension 7157 (except Saturday), or write *promptly* to

NEW YORK HOSPITAL

Surgical Follow-up Department
525 East 68th Street
New York City

If you have moved, notify us of your new address.....

TABLE I

INTERVALS FOR FOLLOW-UP EXAMINATIONS

	1st Visit	2nd Visit	3rd Visit	4th Visit
Appendicitis (acute)	6 mos.	1 yr.		
Appendicitis (chronic)	1 yr.			
Benign breast tumor	6 mos.	18 mos.		
Biliary tract disease	6 mos.	1 yr.	18 mos.	
Brain and cord tumors	6 mos.	1 yr.	1 yr.	Yearly*
Carcinoma of breast	4 mos.	6 mos.	1 yr.	Yearly
Fractures	6 mos.	1 yr.*		
Gastric operations for ulcer	6 mos.	18 mos.	3 yrs.	
Gastric operations for carcinoma	6 mos.	6 mos.	1 yr.	Yearly
Gynecologic operations	6 mos.	1 yr.		
Hernia (all varieties)	6 mos.	18 mos.		
Infections of hand (major)	6 mos.	1 yr.*		
Malignancy of bowel	6 mos.	6 mos.	6 mos.	Yearly
Orthopedic operations	6 mos.	1 yr.		
Other malignant neoplasms	6 mos.	6 mos.	6 mos.	Yearly
Rectal diseases (nonmalignant)	1 yr.			
Tbc. nodes of neck	6 mos.	1 yr.	2 yrs.	
Thoracic operations for empyema	6 mos.	1 yr.		
Thoracic operations for tbc	6 mos.	1 yr.	2 yrs.	5 yrs.
Thyroidectomy (nontoxic)	1 yr.	1 yr.		
Thyroidectomy (toxic)	6 mos.	1 yr.	18 mos.	
Urologic operations:				
Tumors	3 mos.	6 mos.	1 yr.	Yearly
Prostatectomy (benign lesions)	1 yr.	1 yr.	1 yr.	
Stones	6 mos.	1 yr.	1 yr.	
Tbc.	4–6 mos.	6 mos.	1 yr.	1 yr.
Others	1 yr.			
Varicose veins	1 yr.			

* If necessary.

The unsealed envelope costs less to send than a sealed one, but even though it is unsealed, it is a little more dignified and personal than a postcard and eventually it is probably worth the additional cost. But because the envelope is unsealed, it will not be forwarded or returned if not delivered. From 48 per cent of these notices patients respond by coming to the clinic, writing or telephoning. Of the 52 per cent that bring no response, it is estimated one-third of them reach their destination but are unheeded.

Accordingly, to all those from whom there was no response, a second card is sent (white, 6x3½ inches), but this time in a sealed envelope. This notice is as follows:

NEW YORK HOSPITAL

Name.....History No.....
We have had no answer from our request that you return to the Surgical Follow-up Clinic. We wish to see you a few minutes in order that we may observe the result of your treatment in the New York Hospital. We may be able to give you valuable advice and you can help us complete the records of your case.

This service is given free of charge.

Will you please come to the Surgical Follow-up Clinic, 5th Floor, K Bldg., on Sunday morning.....at.....o'clock

Bring this card with you and use the entrance at 516 East 70th Street. If you cannot come, call REgent 4-6000 Extension 7157 (except Saturday), or write *promptly* to

NEW YORK HOSPITAL
Surgical Follow-up Department
525 East 68th Street
New York City

If you have moved, notify us of your new address.....

Thirty per cent of these bring a response of some type. Twenty per cent are returned with a post office stamp of some sort such as, "unclaimed," "unknown," "moved, left no address." The remaining 50 per cent, it is assumed, reached their destination but failed to bring responses from the patients.

To those delinquents, assumed to have received the previous notice or notices, the letter on the next page is sent in a sealed envelope together with a Business Reply envelope for its return. From 40 per cent of these some response is obtained.

The group of patients that remains uncontacted is comprised of those whose notices were returned by the Postal Department and those who obviously received notices but failed to respond. The secretary now peruses the patient's hospital chart for telephone numbers, names and addresses of relatives, friends, referring doctors, clubs, churches, insurance companies, schools, *etc.* One or all of these in turn are phoned or written to in the hope of reaching the patient or getting information about him. A form letter as follows

Dear

We have sent you two requests to come to the Sunday morning Surgical Follow-up Clinic and have had no reply. We are very anxious to know your progress since you left the New York Hospital, and if possible, we should like to examine you. By such a check-up we might be able to give you valuable advice, and it would also help us to complete the record of your illness. If, however, you feel that you cannot or do not want to come to the Clinic, will you kindly cooperate with us by answering the following questions and return this questionnaire to us in the enclosed envelope.

1. If you have moved, what is your new address?
2. Do you feel that the symptoms for which you were treated have been cured, improved, or unimproved?
3. If you have any new complaints, what are they?
4. If you have had any other treatment of what did it consist?
5. Please write any other points of interest about your health.

Yours very truly,
Surgeon-in-Chief

is frequently used for this purpose, and with it is enclosed a Business Reply envelope:

Dear

We should like to learn the condition and whereabouts of a former patient of ours. We wish this patient to attend our Sunday Surgical Follow-up Clinic so that we may check the results of our treatment. This service is given free of charge and would be of considerable value to the patient as well as to us.

Every effort has been made to locate the patient, but without success. Any information you could give us would be greatly appreciated.

Yours very truly,
Surgical Follow-up Dep't.
Room 1104

Favorable response of one type or another from these attempts is obtained for about 40 per cent of this group of patients. If there is good reason for suspecting that the patient has died, the Bureau of Statistics of the Board of Health may be of aid in verifying the suspicion.

After all these attempts, a group is still left of whom there is no information, and this group is turned over to a social service worker to investigate. It is little wonder that the worker finds only a small percentage of these patients or gets some word of them (7 per cent), but even this is worth the effort.

Nothing has been said of the out-of-town patients who may be unable to come to a Follow-up Clinic. To these is sent the following questionnaire:

Dear

We are very much interested in your progress since you left the New York Hospital. Owing to the fact that you live out of town and perhaps cannot conveniently arrange to return to the Hospital for examination, would you be good enough to answer the following questions:

1. If you have moved, what is your new address?
2. Do you feel that the symptoms for which you were treated have been cured, improved, or unimproved?
3. If you have any new complaints, what are they?
4. If you have had any other treatment of what did it consist?
5. Please write any other points of interest about your health.

Yours very truly,
Surgeon-in-Chief

When there is no response, somewhat the same procedure as outlined above is employed to get word of the patient. Where necessary or feasible, a cooperative out-of-town patient is asked to consult a local physician at intervals and a report requested from the physician. It is frequently necessary to send an abstract of the case to such a physician who may be unacquainted with the facts.

In every instance where it is found a patient has died, an attempt is made to find out the details of death and get a complete report if an autopsy was performed.

Finally, the cases are closed with (1) "satisfactory follow-up," or (2) "unsatisfactory follow-up." Cases in the first group are those who have reported at the prescribed times or have died and on whom there is a sufficiently complete record. Cases in the second group are those about whom there is no information or only incomplete information.

When the case is closed, the "date card" is destroyed, but the "name card" is removed from the file of current cases and placed in a separate file for closed cases. This file of closed cases has little value except perhaps for purposes of rechecking work. It is to be remembered that the patient's hospital chart contains all of the previously mentioned information in complete form. The examining physician's notes will have been made in the chart; the secretary will have noted all correspondence there; and important letters will have been incorporated in it. When it is necessary to close a case "unsatisfactory follow-up," the chart is stamped with a request to notify the Surgical Follow-up Department if the patient returns to any other department of the hospital or if any contact is made with him.

It is useful in the administration of a Follow-up Department to carry a routine statistical report which incorporates (1) a case census record or "case load" and (2) a work record, for each week. Its function is to give

the administrative heads of the department an idea of the current number of patients being followed, the essential results of the efforts of the department and the work required in the process. This allows for intelligent decision on the need for special studies and revision of policies. Table II is a sample of such a statistical sheet. It actually requires very little time in composing and the ramifications of its value are many.

TABLE II

STATISTICAL TABULATION OF WEEKLY CENSUS

January 3, 1937

CURRENT CASE LOAD

Opening Census:		
Census brought forward		5,132
New patients referred to Dept.		59
Readmission to Dept.		3
Total		5,194
Discharges:		
(*a*) Successful follow-up completed	37	
(*a*) Deaths	4	41
(*b*) Closed—incomplete follow-up	3	
(*b*) Closed—not found	7	10
Total		51
Closing Census:		
Opening census minus discharges		5,143

CLOSED CASES IN FILE

Opening Census:	
Satisfactory follow-up	2,601
Unsatisfactory follow-up	641
Total	3,242
Closing Census (Opening census plus week's discharges):	
(*a*) Satisfactory follow-up	2,642
(*b*) Unsatisfactory follow-up	651
Total	3,293

RECORD OF WORK

Follow-up Notices:	
First notices	230
Second notices	110
Third notices	50
Other correspondence	25
Phone calls	20
Refers to Social Service	11
Total	446

Response to Notices:	
Attendance at Sunday Clinic	118
Answers by mail	45
Answers by telephone	20
Follow-up exams outside Sunday Clinic	8
Reported by Social Service	2
Total	193
Refers:	
To—O. P. D., B. M. R., Roentgen ray, *etc.*	24
Readmission to hospital	2
Hours of Work:	
Doctor—hours	11–2½
Nurse—hours	2–2½
Nurses' aid—hours	2–3

This statistical sheet is a copy of the one for the week ending January 3, 1937, and expresses the summation of the cases since the work was begun four years previously. It shows that there is a total current case load of 5,143 cases, *i.e.*, cases which are still being followed, while 3,293 cases are closed. 80.2 per cent of the closed cases have been closed with a satisfactory follow-up, while 19.8 per cent of them are closed with an unsatisfactory one (6.4 per cent with incomplete follow-up and 13.4 per cent not found). The total numbers of all cases will steadily increase and perhaps the percentage of cases closed with satisfactory follow-up can be bettered, but there will always remain that small group of patients who will not cooperate and that group who mysteriously disappear. It has been interesting to note that studies of special groups of cases have shown much higher percentages of satisfactory follow-up for them than the general average of 80.2 per cent quoted for all cases. For example, 95 per cent satisfactory follow-up occurs to date in all types of carcinoma cases, 92 per cent in thyroid cases and 85 per cent in hernia cases. The percentages fall below the average in the many minor surgical conditions we feel it necessary to follow, such as hemorrhoids, fistulae, fractures, *etc.*

The business of analyzing operative results is not a function of the Follow-up Department. Such results should, or can rarely, be expressed in a word as good, fair or poor, but require greater consideration and call for special studies. For example, in classifying results of even such simple cases as hernioplasties, the terms good, fair and poor result in only superficial analysis. These terms might be used to designate respectively cures, questionable cures, and recurrences; however, one should be interested not alone in cures or recurrences, but also in the condition of the cord, the testicle, the ring, questions of local discomfort and effects on the patient's well being and his ability to work. Incomplete summaries of results are to be discouraged as not representative of careful and valuable work. From this standpoint, it is solely the aim of the Follow-up Department to make possible

the recording of worthwhile notes in the patient's hospital chart during the follow-up period. This accomplished, the charts are ready for careful and unbiased investigation in special studies to be made from time to time by the staff members.

The expenses involved in maintaining such a department are mainly the salaries of the secretaries and the costs of stationery, secretarial supplies and postage. A glance at the statistical sheet above will give an idea of the number of patients handled and the bulk of work required. An itemized estimate of the cost of carrying on this work for a year is as follows:

Secretaries' salaries	$2,500.00
Cost of stationery and supplies for approximately 13,500 notices, letters, *etc.*	100.00
Cost of postage for this amount of correspondence	250.00
Total	$2,850.00

There are, in addition, moderate expenses such as laundry, heat and light for the Sunday Follow-up Clinic, and the telephone which are all automatically included in the general hospital budget. The services of social service workers, nurses and doctors should be forthcoming without additional cost.

All this organization, detail and expense may not appear on the surface to be necessary or perhaps worth the effort in terms of results, but it is an assured fact that unless such pains be taken, results will suffer accordingly. Of course, one must first of all be convinced of the necessity or desirability for this kind of work. It is not the purpose of this paper to argue these points, though in viewing the matter from one angle, one has only to work in this field for a short time to discover how appreciative the patient is of this attention; how it serves to establish ties between him and the physician and the hospital; how the physician, young or old, is made aware of a valuable long time view of his work; and finally, how a hospital can serve its community and staff in a finished manner.

ABSCESS OF THE TONGUE

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ABSCESS of the tongue is rarely encountered, but the fact that it caused three deaths in the first series of cases[1] collected is reason enough why instances should be reported, and attention called to its diagnosis and treatment. No deaths have been reported since Bennet's original article in which he cited 145 cases (1816–1909).

During the past 20 years ten cases[2, 3, 4, 5, 6, 7, 8, 9] have appeared in the American and 20 in the foreign literature. To these we wish to add a recent case personally observed (G. P. G.), and another from the service of Dr. Irvin Abell at St. Joseph's Hospital, which he treated in 1921, and which was the only other instance found in a search of all the Louisville hospital records available.

One must remark, however, its relative infrequence in contrast to the abundance of cases of infections of the tonsils, the nasopharynx and the floor of the mouth that are encountered. The tongue is situated in an environment of great potentiality as far as chance of infection is concerned. The normal and active flora of the mouth provides innumerable sources of infection, yet the tongue, apparently, does not become involved very often.

This may be explained because: First, the mucosa of the tongue has a specialized and unusual firmness because of the large amount of cornified epithelium that is present at the summits of the filiform papillae. Second, each of these papillae has multiple secondary papillae of firm connective tissue and each has an independent and abundant blood supply. Third, the amount of submucous areolar tissue is conspicuous by its scarcity. Fourth, the musculature is of the most compact arrangement, also with a very abundant blood supply. Fifth, the fact that suppuration does not involve muscle tissue, but displaces it.

CASE REPORTS

Case 1.—C. W., a white male, age 45, laborer, had been subject to frequent attacks of tonsillitis for several years. His present condition was initiated by another attack of tonsillitis, which, however, after persisting for five or six weeks, was followed in about two weeks by soreness under the right, and later the left lower jaw. A few days later he noticed that his tongue was becoming larger, became red and began to throb. Within a week it became so large and painful that he had been unable to swallow food for three days, and could not even drink water for one day before he was admitted to the Baptist Hospital.

Physical Examination.—The patient was acutely ill, and markedly dehydrated. His mouth was wide open, and from it protruded an enormously enlarged tongue. Except for an enlarged left submaxillary gland there was no cervical or regional involvement. The

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tongue was practically against the roof of the mouth allowing just one finger to be introduced. Digital examination found the entire tongue involved in a fluctuating mass.

Temperature 104° F., pulse 120. Urine contained a trace of albumin and an occasional granular cast. Blood examination showed 84 per cent hemoglobin (Sahli); 4,530,000 red blood cells; 17,700 white blood cells; differential count 87 polymorphonuclears of which six were young forms, nine lymphocytes and four monocytes.

Operation.—Under local infiltration with novocain, an incision was made at the base of the tongue on the left and a blunt artery forceps was used to spread the edges, revealing a large abscess cavity from which six ounces of foul-smelling pus (odor resembling *B. coli*) were evacuated. Digital examination of the cavity confirmed the fact that the entire organ was involved. A rubber cigarette drain was left in the cavity.

All distressing symptoms were immediately relieved. Postoperative care consisted of frequent hot saline irrigations. The patient was able to swallow fluids immediately. On the third postoperative day the discharge ceased and on the fifth day the patient left the hospital with practically no swelling, able to swallow food without discomfort, and with the wound healed.

Smear of the pus showed fusiform bacilli and spirochetes and a gram-positive coccus. Cultures did not grow on ordinary aerobic media.

Case 2.—Doctor Abell[10]: A white male, age 35, who said he thought he had had a sore throat for five weeks before he noticed that a swelling had appeared on the posterior right half of his tongue. He gave no history of injury to the tongue. His previous health had been good.

For five days previous to admission to the hospital the swelling had gradually become larger and more tender and he could not swallow food because of the intense pain which had already kept him awake for the three preceding nights.

Except for the local findings of a very tender mass in the right posterior tongue and a palpable submaxillary gland, the examination was negative. Temperature 99° F., pulse 80. Urine showed only a trace of albumin. White blood count 10,700.

The swelling was aspirated and a foul-smelling pus obtained. An incision was made along the right posterolateral border of the tongue from which a half ounce of pus was evacuated. The cavity was drained with rubber tissue held in place with a catgut suture. The patient was discharged three days later after an uneventful recovery.

Discussions.—In Bennett's report the condition is found qually prevalent at all ages. Butlin,[11] however, says it is more common in adults and in males, and in the 12 cases reviewed here all the patients were males, the youngest 34, the oldest 60. No seasonal variance was noted although other reports state that it is more common during the winter.

Exposure is found to be the most common predisposing factor. Sore throat, tonsillitis, and such diseases as typhoid, variola, erysipelas and thrush have been mentioned as etiologic factors in specific cases. Mahoney[9] reports (the last two cases reported in the United States) one case eight days after a tonsillectomy and another five days after a molar extraction. The last reported case (Syme[12] of London) gives no clue to the etiology whatsoever. Erosions within the mouth, salivary gland infections, wounds caused by dental appliances or jagged teeth, burns and other physical and chemical agents have all been held responsible. Loeb[13] reported a case due to scratches on the tongue from chewing sticks of pine wood. Raynor's[14] case occurred following a submucous resection.

It is easy to understand the mode of infection in cases due to direct

trauma in the presence of bacteria, but the other instances that cannot be accounted for in this manner must be attributed to lymphatic or blood stream transportation.

Bacteriologically, all reports are deficient. Mixed infections of staphylococcus, streptococcus, diphtheroids and anaerobic bacteria are the most common organisms recovered. Most uniform, however, is the fact that the pus is always foul smelling.

From what we know of the anatomy and histology of the lingual septum which divides the organ into halves, it would appear that the majority of cases would be confined to one side. This is true of 11 of the 12 reviewed here. The one exception is Case 1 herewith reported. On the other hand, Bennet's large series shows the entire organ involved 85 times.

A description of any of the cases reported is representative. The onset is insidious, the prodromal symptoms being those of the antecedent infection. Occasionally, after the abscess has formed it will enter an acute stage with chills and septic temperature.

The symptomatology consists, in the main, of pain in the tongue and dysphagia, with referred pain to the jaw and occasionally to the head and ear, the latter when the chorda tympani is involved. In Hansel's[7] case he was able to control the pain in the ear, which was the first symptom, by injecting one drop of novocain into the nasal ganglion. He repeated this until the abscess fluctuated, which was then incised. The tongue will swell, at times filling the entire oral cavity, and interfering not only with deglutition but with breathing and speech also. In the beginning the mass is hard, but becomes fluctuant after suppuration takes place.

The diagnosis is not difficult. The condition is to be differentiated chiefly from:

(*a*) Actinomycosis: The onset is much slower, the course longer, there is no extreme pain, a sinus frequently forms and the sulphur bodies and ray fungus may be easily identified in the discharge.

(*b*) Allergic macroglossia[15]: This occurs suddenly and may or may not be accompanied by a skin lesion. It may last several hours to several days.

(*c*) Anthrax: There is more necrosis, discharge is bloody and again the organism very definite.

(*d*) Leprosy: There is usually an area of anesthesia, and the general signs of the infection.

(*e*) Salivary gland calculus: This may occur either in the submental or submaxillary glands. The pain is not quite as marked as in abscess of the tongue, although it may cause a sympathetic macroglossia. The calculus can usually be palpated and expelled.

(*f*) Stomatitis: This is often accompanied by macroglossia, especially when it is generalized and accompanying Ludwig's angina, pemphigus, scurvy, the exathematous fevers, erysipelas or herpes zoster.

(*g*) Syphilis: Gumma of the tongue is not painful, the swelling remains

firm and well circumscribed in contrast to the parenchymatous glossitis that accompanies an abscess. There are also the general signs of the infection.

CONCLUSIONS

Abscess of the tongue calls for prompt and adequate incision. Ice chips held in the mouth, strict oral hygiene, frequent irrigations and good nursing are essential.

Each case must be carefully evaluated before general anesthesia is used in lieu of local infiltration because of the precarious condition of the tissues surrounding the entrance to the main air passages that accompanies this condition.

A posterolateral incision is preferred because it allows quicker healing, there is less chance of hemorrhage, and if the latter should occur it can be controlled by suture here more easily.

In the 12 cases I have reviewed there have been no complications or deaths. In a previously reported group (Bennet's) three deaths were reported caused by: (1) Aspiration pneumonia when an abscess ruptured spontaneously. (2) Acute edema of the glottis. (3) Hemorrhage.

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ENDOBRONCHIAL PROBING COMBINED WITH SERIAL SELECTIVE BRONCHOGRAPHY FLUOROSCOPICALLY CONTROLLED

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IN 1921 Sicard and Forestier[1] introduced iodized oil as a roentgenographic contrast medium. During the next year these authors[2] with Leroux[3] employed it for bronchography. Throughout the past 15 years several methods to visualize the bronchial tree by means of radiopaque oils were devised. At first the methods differed chiefly according to the technic developed for allowing the oil to reach the bronchial tree beyond the protecting sensitive larynx, *i.e.*, subglottic,[2, 3, 4, 5] supraglottic,[6, 7, 8] intratracheal catheter,[9, 10, 11, 12] and bronchoscopic.[13, 14, 15, 16, 17, 18] Later, methods were used which gave more control of the bronchograph.[19, 20] Thompson's[21] bronchial catheter has made possible additional refinements in technic.

Recently, a bronchographic technic has been developed which has given clearer answers to many diagnostic problems presented to this thoracic surgery clinic. The purpose of this paper is to describe this method of endobronchial probing with serial selective bronchography fluoroscopically controlled. A few illustrations of its use in some surgical diseases of the chest will be cited.

Apparatus and Equipment.—Two types of catheters are needed: large bored, rubber, radiopaque Thompson[21, 22] bronchial catheters with various curves to the tip (Fig. 1, Nos. 2, 3 and 4), and ureteral catheters of different sizes, also radiopaque (Fig. 1, Nos. 3 and 5). Palpable markers are placed at two points measured from the tip of the ureteral catheters (Fig. 1, No. 5), the proximal one at a distance equal to the length of the bronchial catheter, and the distal one 5 cm. longer. These palpable markers enable the operator, in the darkness of the fluoroscopic room, to estimate the distance that the smaller catheter is inserted beyond the larger one. A semirigid, malleable, metal stillette or introducer (Fig. 1, No. 1) is used to thread the bronchial catheter through the epiglottic ring. A special high pressure metal syringe facilitates injections of the oil through the ureteral catheters (Fig. 1, No. 5).

The roentgenographic apparatus consists of a combination fluoroscopic and roentgenographic unit mounted on a tilt-table in an isolated room. Six feet away from the tube is an upright cassette holder for taking films at that distance. High speed cassettes 5x7 to 14x17 inches are used. Conversion from fluoroscopic to roentgenographic unit is made by throwing the "quick switch" which is conveniently located within the fluoroscopic room.

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Technic.—The patient is prepared for the exploration with a suitable dose of phenobarbital given one and one-half hours before starting the cocainization. This is a specific antidote to the toxic effects of cocaine and supplies sedation. The examinations are usually made in the afternoon in order to allow time for postural drainage and clearing the bronchial tree of secretions. Lunch is omitted and the patient instructed to take no food or drink after breakfast.

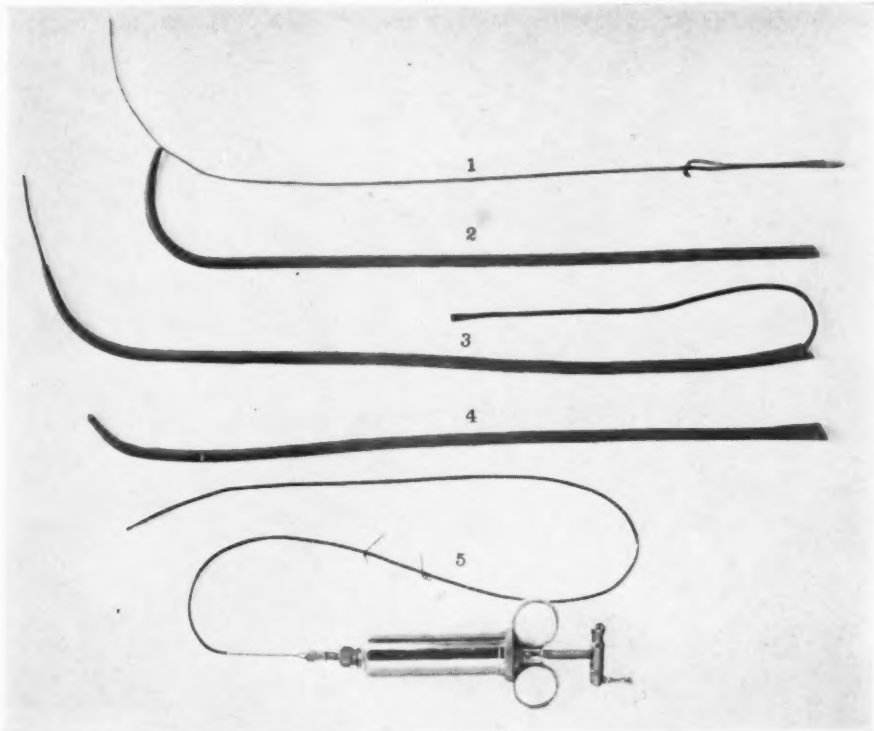

FIG. 1.—Catheters and syringe for endobronchial probing with serial, selective bronchography, fluoroscopically controlled. (1) Semirigid, malleable, metal stillette. (2), (3), and (4) Thompson bronchial catheters. (3) Contains ureteral catheter as for probing. (5) Shows metal syringe attached to ureteral catheter which has palpable markers.

The actual technic of exploring the tracheobronchial tree involves four steps: (1) Anesthesia; (2) introduction of catheters and endobronchial probing; (3) exploration with contrast medium; and (4) permanent confirmatory recording by means of "spot-film" and routine technic. These four steps may overlap but for the sake of description they are best separated.

Anesthesia.—Cocaine hydrochloride is used as a mucous membrane anesthesia. Ten per cent solution is applied with moderate pressure to the pharynx, soft palate, and pyriform fossae by means of cotton swabs. Under mirror vision the larynx is swabbed with 2 per cent cocaine. During these acts the patient is encouraged to cough up any secretions and instructed not to swallow.

When the larynx can be swabbed without inducing cough the patient is given a few minutes' rest while the operator instructs him what is about

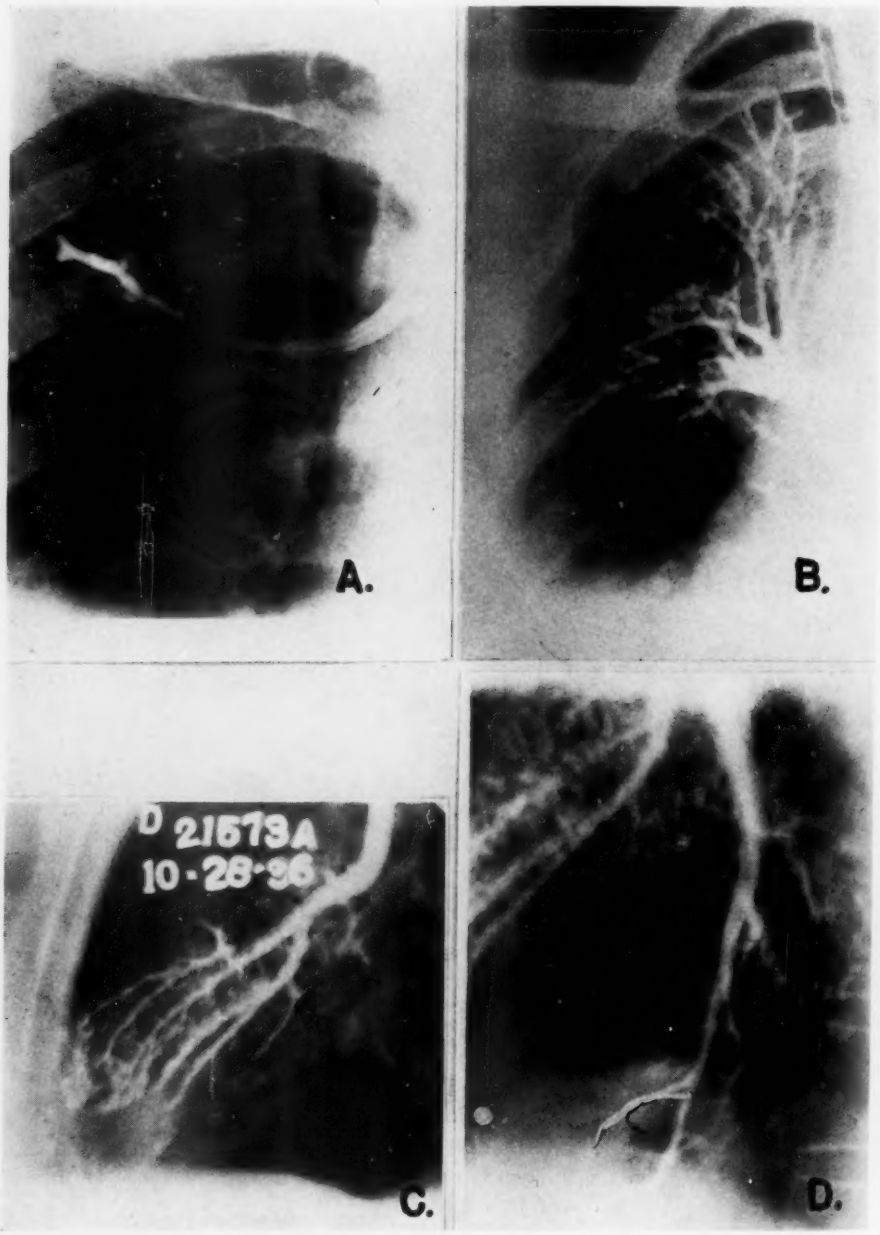

FIG. 2.—Positions of catheters in normal lung and serial selective "spot-films" of the bronchograph. (A) Injection of isolated peripheral bronchus of fourth and fifth order in right upper lobe made through ureteral catheter. (B) Ureteral catheter removed and remainder of lobe filled through the bronchial catheter. (C) Lateral view showing catheter in right middle lobe. (D) Catheter slipped from right middle into right lower lobe, paramediastinal branch. The lower mesial portion of right middle lobe is also seen.

to take place so that his cooperation may be gained, since the voluntary cough is never abolished.

Introduction of Catheters and Endobronchial Probing.—The proper bronchial catheter is mounted on the introducer and the tip placed through the epiglottic ring under mirror vision. By unthreading the catheter from the stillette the tip of the former is made to pass through the larynx and lies in the trachea. This may incite cough which is controlled by the instillation of from 3 to 6 cm. of 2 per cent cocaine. Anesthesia of the trachea and main lobar bronchi is usually accomplished with this procedure. In some cases the

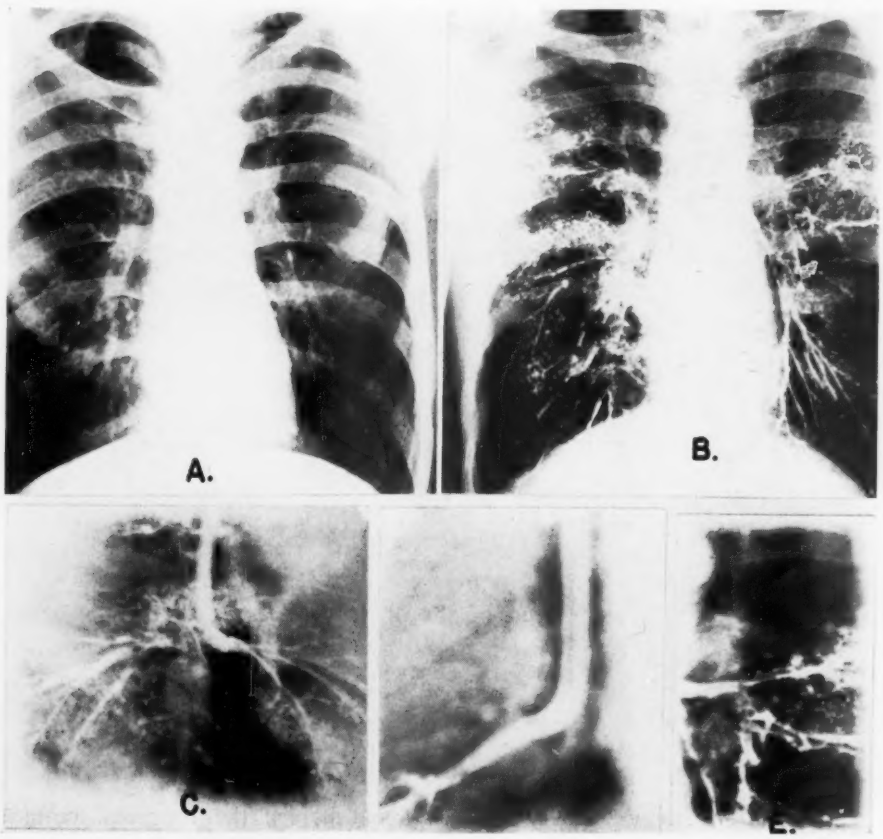

FIG. 3.—T. E. Male, age 30. Chronic cough, sputum, intermittent dyspnea. (A) Plain roentgenogram indefinite but suggestive of fibrosis, emphysema, and bronchiectasis. (B) Finished bronchograph with partial exploration of all lobes. (C) Catheter in right middle lobe, just removed from segment of right lower lobe—note relation of right middle lobe to this segment. Lateral view. (D) Oblique view of catheter in right middle lobe. (E) Catheter in left upper lobe just removed from left lower lobe. Note the descending branches to lingula of left upper lobe. This appears to be a case of emphysema, fibrosis, and secondary bronchial changes; obviously not surgical.

2 per cent cocaine is instilled directly into the catheterized lobar bronchi. The ureteral catheter is now inserted into the bronchial one and the remainder of the exploration carried out under fluoroscopic control. After a five minute wait for the cocaine to take full effect, the patient is placed in a supine position on the fluoroscopic tilt-table, which is at an angle of 15 to 45 degrees.

With just the tip of the bronchial catheter inserted into the desired main lobar bronchus, the ureteral catheter is pushed slowly beyond the end of the bronchial sound and lies in a branch bronchus of that lobe. By gentle manipulation of the distal end of the bronchial catheter, its tip and consequently the ureteral catheter may be pointed in various directions. Sounding with the ureteral catheter allows any accessible unobstructed or partially obstructed branch bronchus to be probed. The details of an isolated peripheral branch may be shown after the instillation of a drop or two of iodized oil (Fig. 2, A). The meeting of an obstruction requires an injection of a small amount of iodized oil to outline that obstruction (Fig. 6, D), and thus may guide further probing. The fluoroscopist may at any time take a "spot-film" to record the position of the ureteral catheter (Fig. 2, A). By successive manipulations the entire bronchial tree may be explored (Figs. 3, B, and 4, E). Although some cases do not need endobronchial probing, often the information obtained enables the operator to select certain areas for injection and exclude others. When the endobronchial probing has been evaluated, the contrast medium may be instilled.

Exploration with Contrast Medium.—The syringe is loaded with the preheated (37° C.) iodized oil. If a single bronchial segment[23] is to be injected, the bronchial or the ureteral catheter may be used (Figs. 2, D, 3, C, and 2, A). Bronchi of the fourth and fifth order may be studied singly (Fig. 2, A) by injecting the oil through the ureteral catheter. It may be decided to fill an entire lobe more rapidly (Figs. 2, B, C, and 4, B, C), in which case the ureteral catheter is entirely withdrawn and larger amounts of iodized oil instilled through the bronchial catheter. All injections of oil are made very slowly, each few drops being allowed to spread over the bronchial mucosa before injecting further. If the patient is asked to take a deep inspiration or a forced expiration, the spread may be made more rapid. It is highly desirable to avoid spread of the oil into the alveoli. The complete outlining of cysts, cavities, and irregularities of bronchial lumina is often facilitated by the use of the tilt-table (Fig. 4, compare C and E). Then, too, with changes of position a large area within the catheterized lobe may be outlined with a relatively small amount of oil. It is advantageous at times to instill oil during the endobronchial probing. Upon the fluoroscopic demonstration of pathology "spot-films" are taken before the bronchial pattern becomes obscured by clouds of scattered lipiodol in bronchioles and alveoli (Fig. 4, compare A and E). Cough and overfilling are the main causes of bronchiolar and alveolar filling. These are readily avoided with this technic by adequate anesthesia and slow instillation fluoroscopically controlled. As long as scattering is controlled, the exploration with contrast medium may proceed in a leisurely manner, with a loaded cassette ever ready for "spot-filming."

Spot-filming.—Before cocainization, the patient is routinely examined and fluoroscopy of the chest performed. A "spot-film" of the area to be studied,

taken at this time, is developed while the local anesthesia is being applied. This is examined immediately and serves as a guide to the correct KVP setting. The fluoroscopic settings are 4 Ma. stabilized current at KVP from 40 to 60 depending upon the pathology and thickness of the chest. Throwing the "quick switch" converts the factors to 50 Ma. stabilized current at same KVP and places the automatic timer in series. Exposure is made by placing the loaded cassette over the area outlined by the shutters and pressing the

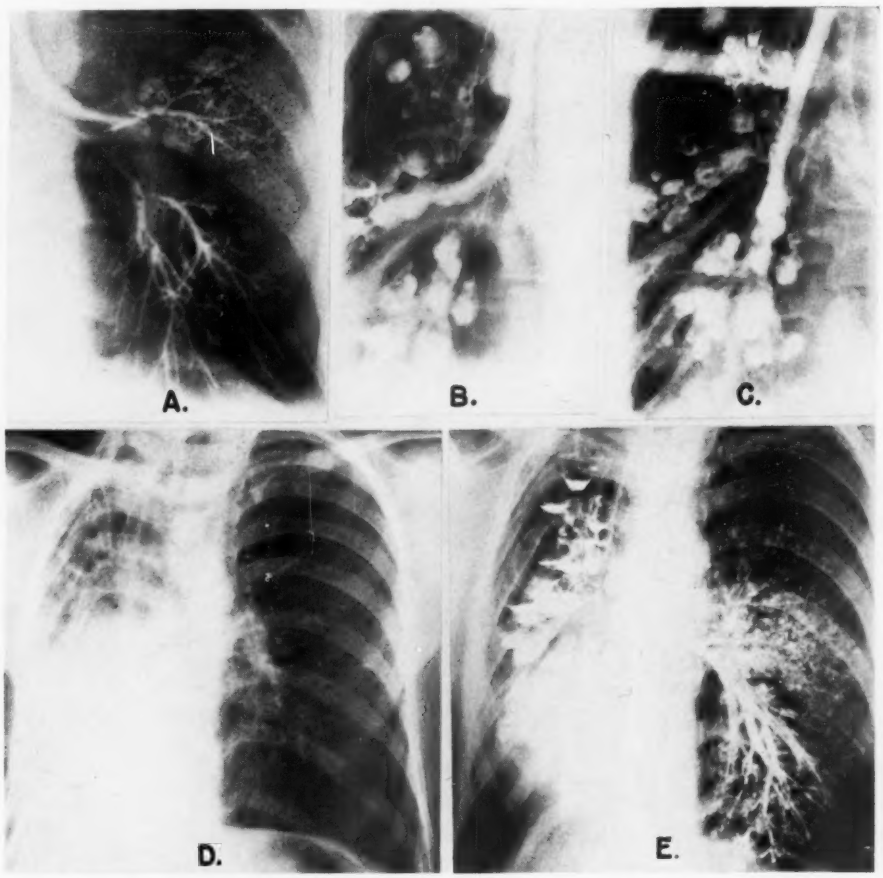

FIG. 4.—T. J. Male, age 19. Bronchopneumonia severe, nine months previously, with persistent cough thereafter. Frequent exacerbations of increased cough, sputum and fever, usually diagnosed pneumonia. Underweight, marked psychologic changes. Sauerbruch type thoracoplasty, 1927. Persistence of symptoms. Bronchography, November, 1936. (A) Catheter in left upper lobe after injection of left lower. Note left upper lobe lingula overlying left lower lobe bronchi. Normal bronchi on left side. (B) Catheter in right upper lobe; some iodized oil has leaked into lower portion of lung. Cystic bronchiectasis. (C) Catheter in right middle lobe, more complete injection. Dilatations in lower lobe in background. (D) Plain roentgenogram showing obscuring of pathology in lower right chest by chronic inflammatory changes. Cystic bronchiectasis can be diagnosed in upper portion. Heart in right chest. (E) Completed bronchograph. Note increase scattering in left lung, and change in outline of cysts as patient moved to upright position.

fluoroscopic foot switch. One-twentieth, 1/10, and 3/20 seconds are used for postero-anterior, oblique, and lateral views, respectively.

At any point in the exploration when permanent roentgenographic records

TABLE I

COMPARISON OF BRONCHOGRAPHIC METHODS

	Control of Cough	*Control of Patient's Position*	*Control of Oil*	*Control of Roentgenogram (Bronchograph)*
Subglottic	Incomplete: Adequate anesthesia difficult to obtain Moving oil in contact with large area of sensitive mucosa	Must be in dependent posture as regards area to be filled May require several changes of position	Below larynx by gravity Amount excessive Subject to dissemination by cough	Relatively nonselective
Supraglottic	Incomplete: Adequate anesthesia difficult to obtain Moving oil in contact with large area of sensitive mucosa	Must be in dependent posture as regards area to be filled May require several changes of position	Below pharynx by gravity Amount excessive Subject to dissemination by cough	Relatively nonselective
Intratracheal catheter	Complete	Dependent position only as regards relation of stem bronchus to lobar bronchus Fewer changes of position	Below main stem bronchi by gravity Amount less Less subject to dissemination by cough	Selective
Bronchoscopic	Incomplete: Untrained patient tense and nervous Metal instrument in contact with mucosa	Position limited by bronchoscope	Amount less but empiric	Selective
Endobronchial probing with serial selective bronchography fluoroscopically controlled	Complete: Anesthesia adequate No moving oil in contact with sensitive mucosa	Full freedom. No limitation by intralobar catheter or gravity Changes of position minimal; attained by tilt-table	Complete: Oil in catheter until actual area of exploration reached Any bronchus accessible Catheter in bronchus helps prevent spread by cough	Completely selective Fluoroscopic control "Spot-film" recording

are desired, a suitable cassette is placed between patient and fluoroscopic screen, the "quick switch" is thrown and the patient told to hold his breath while the fluoroscopic foot switch is pressed. This cassette is then removed and another held in readiness as the exploration proceeds. Serial films may be made (Fig. 5, C, E.). Lateral and oblique views are especially desirable for recording location (Figs. 6, C, 3, C, 2, C, D, and 5, D), while certain attitudes may be assumed by the patient to accentuate detail or to bring an

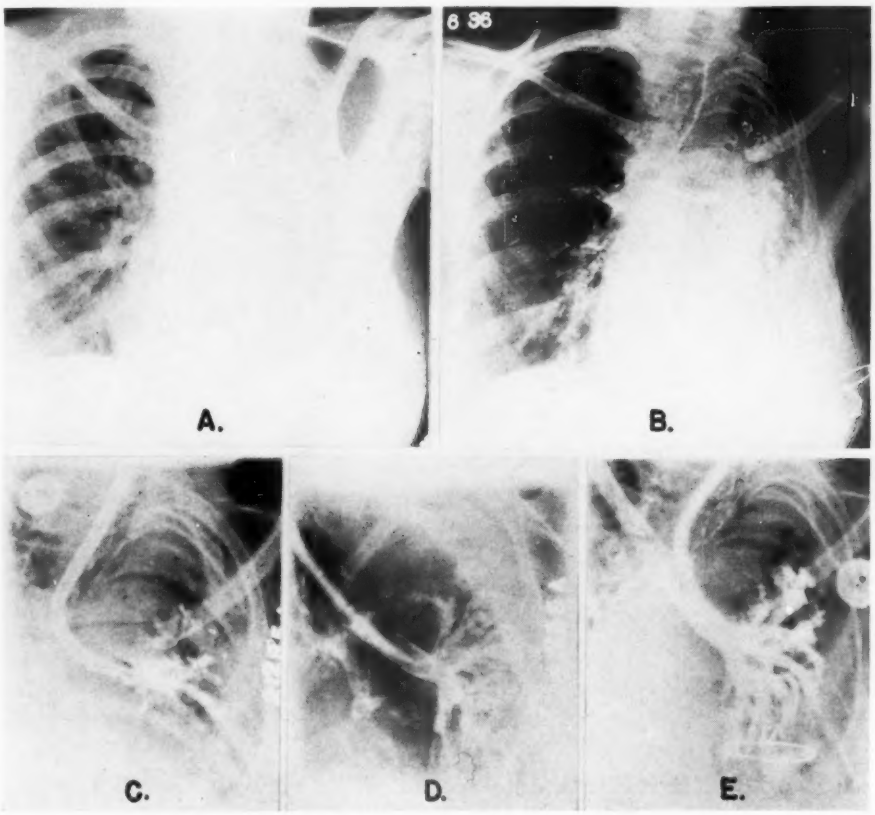

FIG. 5.—C. T. Female, age 33. Rib resection 15 years ago for empyema. Since then recurrent episodes of fever, empyema necessitatis, increased drainage, foul at times, every one or two years. No cough or sputum. Surgical drainage of chronic empyema, October, 1936. Bronchographic exploration, November 6, 1936. (A) Plain roentgenogram fails to show underlying lung because of thickened pleura, fibrosis and atelectasis. (B) Finished bronchograph showing shrinkage of entire left lung, abnormal course and terminations of bronchi without formation of cystic bronchiectasis; no bronchial fistula. (C) and (E) Serial "spot-films" showing degrees of filling. (D) Lateral "spot-film." Note detail and absence of bronchial obstruction. Compare Fig. 6 (D) and (E).

occult area into view, *e.g.*, lordotic posture. In this way fluoroscopically abnormal areas are recorded and confirmed before their appearance is disguised by overlying filled bronchi or lipiodol dispersed with cough (Fig. 7, B, C). Finally routine full chest films are made at six feet to show the finished bronchograph. In certain cases of bilateral exploration the six foot films of a unilateral injection are taken before proceeding to the remaining side.

Comparison of Bronchographic Methods.—The keynote to success in this

method is complete control of the important elements which make an informative bronchograph; namely, cough, position, oil, and roentgenogram (bronchograph). In Table I the four most widely used methods, subglottic, supraglottic, intratracheal catheter, and bronchoscopic, are compared with the described technic.

Control of Cough.—The control of cough is the sine qua non of the per-

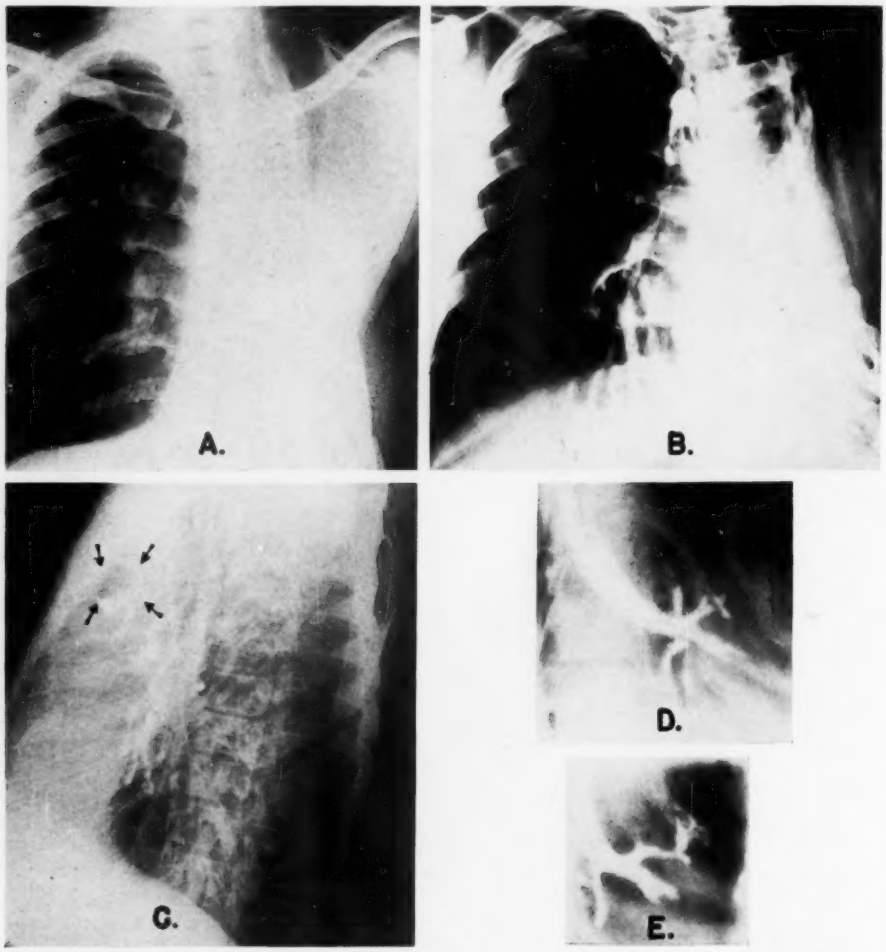

FIG. 6—S. S. Male, age 26. Pulmonary tuberculosis, 12 years' duration. Posterior thoracoplasty, December, 1934. April, 1936, posterior revision, but sputum persisted with an occasional positive on concentration. (A) Plain roentgenogram does not show definite cavity. (B) and (C) Finished bronchograph showing filled cavity seen in (C) to lie anteriorly. (D) "Spot-film" with catheter in left upper lobe. Ureteral catheter stopped by obstruction 1 cm. from tip of bronchial catheter. (E) Shows further filling of a stenotic bronchus leading toward the cavity outlined in (C). No other patent bronchi in upper lobe. Note bronchiectasis in lower lobe when oil outlines these after removal of catheter in (C).

fect bronchograph. From the foregoing description of the technic it can be seen that the control of cough is readily attained. Anesthesia of respiratory mucous membranes is adequate even without completely abolishing the voluntary cough; the more sensitive pharyngeal, laryngeal, tracheal, and bronchial

mucous membrane is protected from contact with a moving stream of oil; the patient is relaxed and in a more or less upright position; movements are free and unhampered by the rubber catheter; the required changes of position are minimal in number; and metal instruments do not come in contact with the respiratory mucous membrane.

Control of Patient's Position.—Full freedom of movement controlled, as much as possible, by passive shifting of position is highly desirable. This is readily accomplished with the fluoroscopic tilt-table. Some methods can-

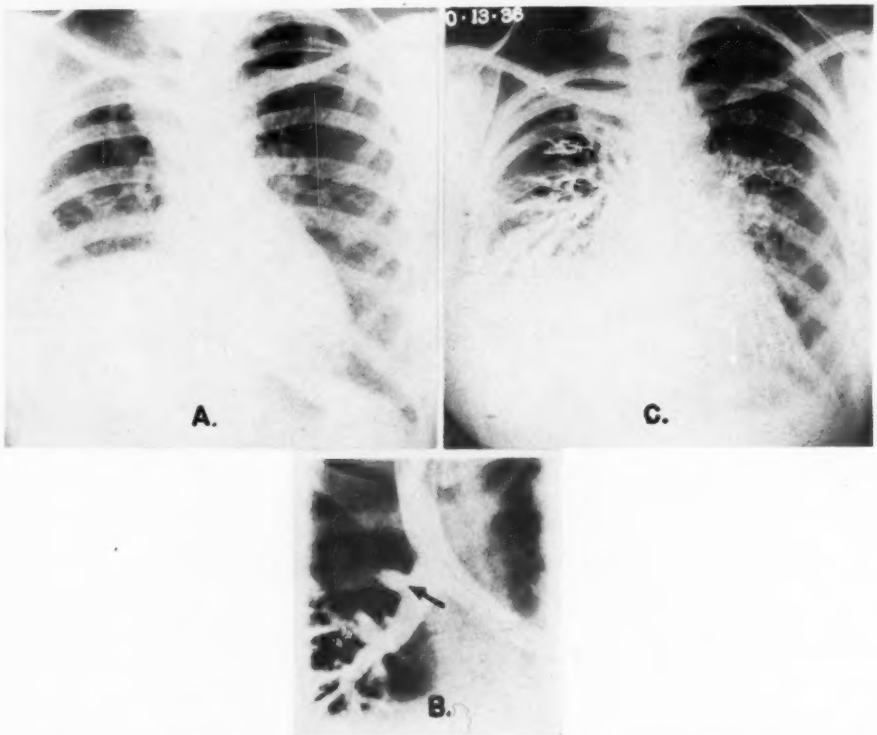

FIG. 7.—E. B. Female, age 19. Pulmonary tuberculosis. Seven years' duration. Right phrenic exeresis, 1932. November 8, 1934. Apical thoracoplasty with Semb apicolysis. Next two years sputum negative, but recurrent episodes of fever, cough, foul sputum every four months. Bronchography, October 13, 1936. (A) Plain roentgenogram showing contracted right upper lobe, apical thoracoplasty, and high right diaphragm. (B) "Spot-film" showing complete obstruction of right upper lobar bronchus. (C) Compare with (B) occluded bronchus to right upper lobe not evident in finished bronchograph. Bronchoscopic drainage and dilatation, right upper lobar bronchus, November, 1936.

not readily be adapted to the tilt-table. Catheter methods can utilize it with benefit. In the technic described there is no limitation of movement with lobar catheterization, and a patient may roll completely over without dislodging the catheter from a middle or even an upper lobe. Because the patient is comfortably reclining and relaxing, time becomes unimportant and the exploration may be made more thoroughly.

Control of Oil.—When the oil is brought directly to the area to be explored and instilled under fluoroscopic control without its having to flow over

a large area in the trachea and stem bronchi, several advantages accrue: (1) The amount of oil necessary is lessened, only one-half to two-thirds that used in previous supraglottic methods. (2) Protection from the disseminating action of cough. (3) Protection from swallowing oil which may be dangerous.[24, 25] (4) Prevention of overfilling. (5) Demonstration of otherwise indistinguishable areas (Figs. 2, A, C, 7, B, and 8, B).

Bronchoscopic instillations not fluoroscopically controlled may give rise to alveolar "pseudo-abscess" opacities[14, 26, 27] or even to persisting subpleural collections (Fig. 9).

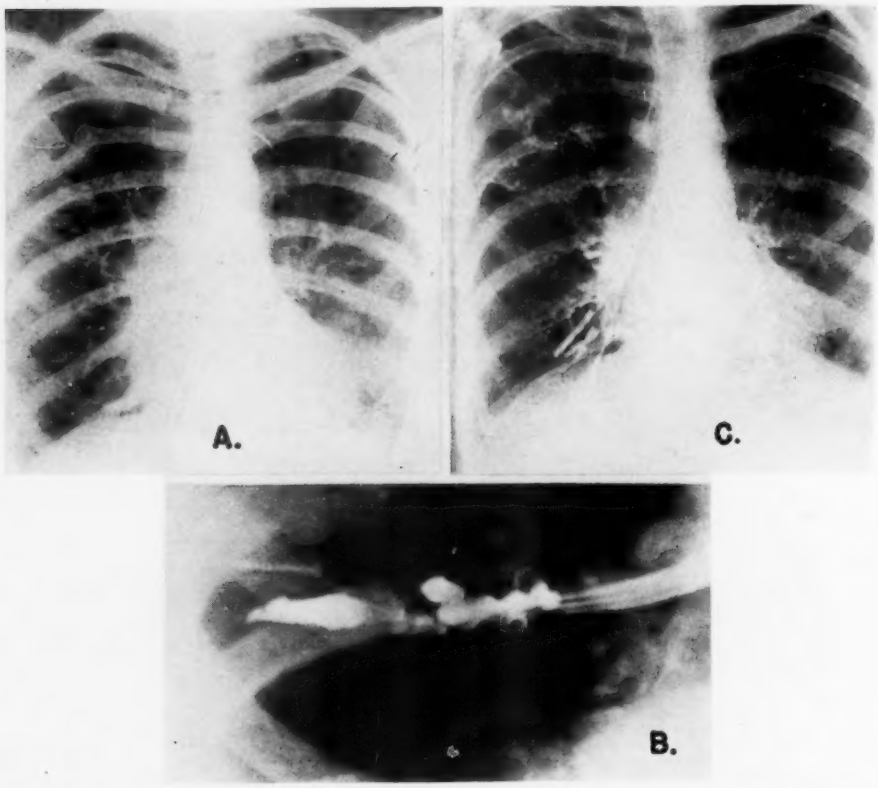

FIG. 8.—F. F. Female, age 26. Whooping cough at age of six, chronic cough thereafter. Lobar pneumonia at 16, complicated by empyema, very ill, protracted drainage necessitating three operations including rib resections. Since then (1926), cough productive, two to three ounces nonfoul sputum daily, some fatigue but doing housework with occasional mild exacerbation. Bronchography, January, 1937. (A) Plain roentgenogram showing area of rib resection in right upper lung field, suggestive areas of bronchiectasis throughout lower two-thirds of this lung. Left lower third also suggestive. (B) "Spot-film" of basal bronchus in right upper lobe filled through ureteral catheter, showing bronchiectatic changes. This anterolateral segment is the only one demonstrated in the right upper lobe. (C) Completed bronchograph showing bronchiectasis right upper lobe, right middle lobe, right lower lobe, and left lower lobe.

Control of Roentgenogram (Bronchograph).—The quality of the roentgenograms depends not only upon the control of the other elements, cough, position, and oil, but also on the selectivity of the filling. This is accomplished by the proper placing of the catheters with the aid of the fluoroscopist's constant suggestions as to their exact location. The use of "spot-filming"

enables the permanent confirmatory roentgenograms to show the pathology in question (Fig. 8, B) before it becomes obscured. When such control is applied to intratracheal catheter methods, excellent roentgenograms may be obtained.[28] On the other hand, it is doubtful that bronchoscopic methods[14] adapted to fluoroscopic control might approach the serial selectivity attained by lobar catheterization, endobronchial probing, and "spot-filming."

Disadvantages.—The described method requires more time and the services of both fluoroscopist and thoracic surgeon, whereas some other methods may require only an operator and a roentgenologic technician. The fluoroscopist should be a well trained roentgenologist.

Dangers.—The potential dangers of instilling an iodized oil into the tracheobronchial tree have been described in detail by Archibald and Brown[25] and others.[29, 30, 31] Many of these dangers are avoided with the described method: (1) Possibility of local sepsis, laryngeal edema, and false passage; (2) dangers accompanying any bronchoscopic procedure; (3) possibility of large quantities of oil reaching the gastro-intestinal tract; (4) danger of transporting infective material from the mouth or larynx by the oil into the pulmonary alveoli; (5) danger of reduction of vital capacity sufficient to produce respiratory embarrassment; and (6) danger of iodism.

Other dangers are avoided by obeying certain contraindications:

(1) Acute Infections.
  (*a*) Upper respiratory.
  (*b*) Bronchopneumonic.
(2) Chronic Infections during Acute Exacerbations.
  (*a*) Bronchiectasis.
  (*b*) Tuberculosis.
  (*c*) Pneumonitis with or without abscess.
(3) Special Conditions.
  (*a*) Acute putrid pulmonary abscess.
  (*b*) Pulmonary tuberculosis which is productive of large numbers of tubercle bacilli in the sputum even though the patient be in good condition or afebrile.
  (*c*) During or immediately following hemoptysis, acute pleurisy, or febrile attack.
  (*d*) Aged, debilitated patients, or infants.
  (*e*) Cardiac decompensation, or low vital capacity.
(4) Patients whose tracheobronchial pathology has been already adequately diagnosed by other means.

At the Massachusetts General Hospital the patients are always seen by the Thoracic Surgery Clinic before a lipiodol instillation is advised.[14] Here the diagnostic problems are threshed out and the indication for the bronchography established. Each case is individually studied so that no hard and fast rules can be laid down. Nevertheless certain indications may be allowed, a few of which are herewith listed.

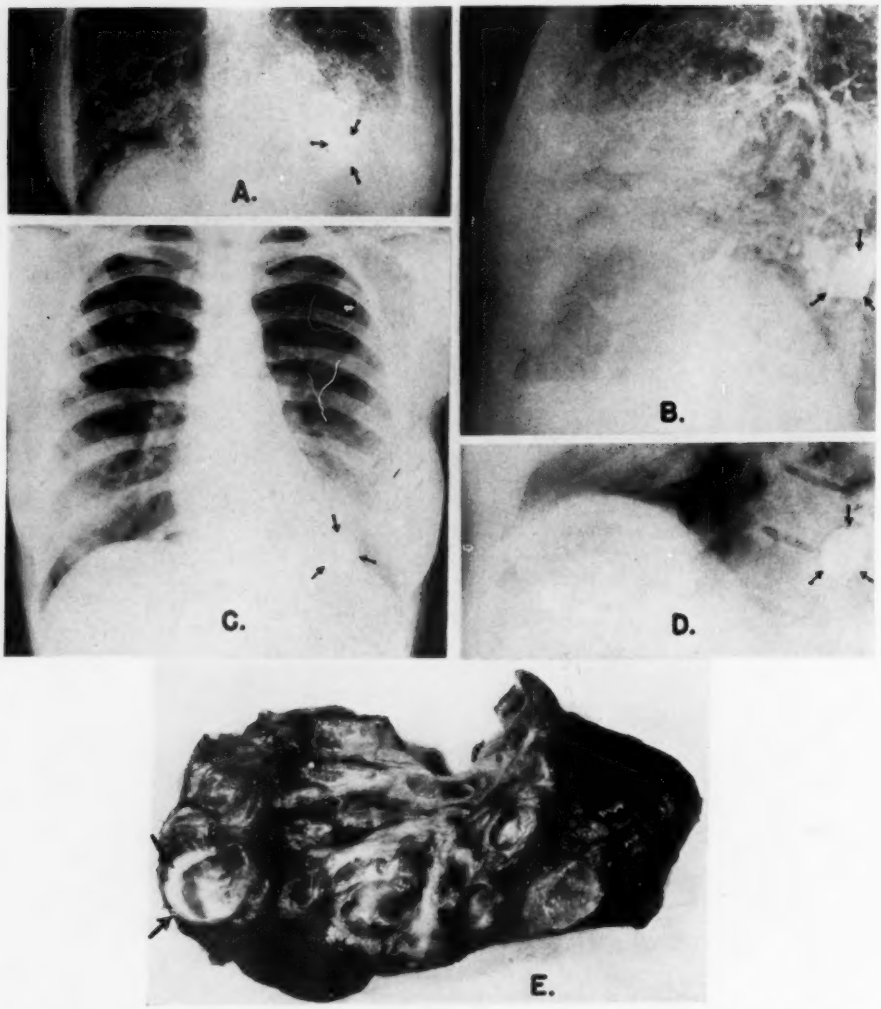

FIG. 9.—M. H. Female, age 26. Combined bronchoscopic and lipiodol examination in 1932. In 1934, cyst of lipiodol remained in left lower lobe. Lobectomy was done. (A), (B), (C), and (D) Cyst of lipiodol under visceral pleura. (E) Resected lobe, opened. Note the isolated subpleural bleb which contained lipiodol.

(1) Bronchiectasis.

(*a*) To prove its presence in collapsed areas, in the lingula of the left upper lobe, and in occult zones.

(*b*) To disprove its presence in the contralateral lung and prove involvement of all lobes in the homologous lung when a pneumonectomy is contemplated (Fig. 4), or to disprove it in the upper lobes when both lowers, with or without the middle lobe, are being considered for bilateral lobectomy (Fig. 8).

(*c*) Patients with history of chronic cough, sputum, febrile attacks, and physical signs suggesting bronchiectasis, but whose plain roentgenograms are indefinite (Fig. 3).

(2) Tuberculosis.
  (*a*) After thoracoplasty to visualize open cavities and demonstrate bronchiectatic changes (Fig. 6).
  (*b*) To demonstrate bronchial obstruction (Fig. 7).
(3) Benign bronchial adenomata—to outline shape, and follow course after treatment.[32]
(4) Differentiation of neoplasm from chronic abscess when bronchoscopy and biopsy are inconclusive.
(5) Demonstration of bronchial obstructions in upper lobes difficult of visualization by bronchoscopy.
(6) Presence of hemoptysis with negative bronchoscopy and negative sputum.
(7) Certain cases of chronic empyema (Figs. 5 and 8).

SUMMARY.—A description of a method of exploration of the lung with iodized oil is given. The control of cough, oil, position of patient and roentgenogram (bronchograph) is emphasized and compared with other methods. Dangers, indications and contraindications are listed.

The use of this technic in solving some of the many problems of diagnosis and treatment arising in a large thoracic surgery clinic is described and illustrated by reproductions of actual roentgenograms with appended histories.

CONCLUSIONS

(1) Endobronchial probing combined with serial, selective bronchography, fluoroscopically controlled, has given better results than other methods in solving certain diagnostic problems confronting the thoracic surgeon.

(2) While bronchoscopy is invaluable for obtaining biopsies, exploration with iodized oil by this method has been found wanting in answering the questions asked by the thoracic surgeon. The described method is *not* a substitute for bronchoscopy.

(3) Endobronchial probing with serial, selective bronchography, fluoroscopically controlled, requires both a roentgenologist and thoracic surgeon.

(4) The described method avoids many of the potential dangers associated with instilling iodized oil into the lung.

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A SUGGESTED METHOD FOR MORE RAPIDLY CURING EMPYEMA

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IN THE past 15 years a voluminous literature on empyema has developed in which almost all phases of the subject have received a very thorough discussion. The one outstanding omission has been the adequate consideration of the factors responsible for the prolonged morbidity despite the various types of treatment advocated for the cure of the disease. Many controversies have occurred over various procedures enthusiastically advanced by different operators for reduction in the mortality rate. These include (a) aspiration advocated by Hamilton Roe[1] in 1844, (b) closed continuous drainage advocated by Cresswell Hewett[2] in 1876, and frequently rediscovered in the last 50 years by various men, (c) open thoracotomy with and without rib resection, (d) irrigation with various types of solution, and (e) air replacement after aspiration. The mortality rates for any single procedure have had wide fluctuations in the hands of different men as a result of which considerable debate has ensued. However, as Graham[3] and Heuer[4] have pointed out, much of this discrepancy in the comparative mortality figures may be the result of marked differences in (a) the ages of the patient in the comparative figures and (b) the years during which the statistics are gathered. It is well known for instance that babies, especially those under the age of one or two years, are more likely to die from empyema than older children and adults, and it has also been shown that there is a great annual variation in mortality of empyema associated with a parallel annual variation in the mortality from the pneumonia. Such matters have received a great deal of attention but little note has been taken of the enormous time lost in the convalescence of the patients who recover. Nor has any direct effort been made to study the causes of morbidity with a view to shortening it.

From 1929 to 1934 we treated 118 cases of empyema by open drainage involving rib resection. We had previously had experience with other methods of treatment but had abandoned them for various reasons, some of which perhaps deserve mention. The closed drainage by aspiration alone is not to be relied upon for reasons best stated by Graham:[5] first, the difficulty of providing adequate drainage because of the presence in the exudate of large masses of fibrin and necrotic tissue which are too large to pass through the needle or the trocar, second, possible harm resulting from the puncture of a lung or blood vessel and, third, the danger of transforming an acute into a chronic case because of continued aspiration over too long a period of time. In a comparative series of cases treated several years earlier by the closed method of drainage

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with irrigation by Dakin's fluid, we found that the convalescent period was considerably longer. This method, in a more complicated form, was advanced by Deryl Hart[6] as valuable because it diminished the convalescent period, but his own results did not seem to indicate that this was accomplished. In this connection it is interesting to note the statement of Rienhoff and Davison[7] following the analysis of cases at the Johns Hopkins Hospital from 1889 to June, 1927, that the mortality rate in infants in whom closed thoracotomy had been performed was nearly twice as high as that in the group in which rib resection was done, and that open thoracotomy with rib resection was a much more satisfactory procedure than closed thoracotomy with a trocar and cannula.

All of our 118 cases were operated upon under spinal anesthesia, and a segment of rib was removed so that the resulting opening was large enough to admit inspection and digital examination immediately after the cavity was thoroughly emptied by suction. Large masses of fibrin were picked out of the pleural cavity with a sponge forceps. (Open thoracotomy and the rapid aspiration of the content by suction on the operating table can be done under spinal anesthesia without any of the dyspnea, sputtering and cyanosis that accompanies a similar attempt under local or other forms of anesthesia.) Then a drainage tube was placed in the cavity and the wound packed. Hygienic measures and dietary regimen calculated to improve convalescence were instituted. No irrigations were given. With the exception of five cases in which there was a markedly prolonged convalescence because of the development of complicating factors, the average duration for 113 of these cases was 45 days from the time the drainage was instituted to the time the wound was healed. No case was discharged from the hospital until wound healing was complete. We have seen cases discharged as cured and sent home with tubes still in the chest. Such cases, of course, deserve no place in a statistical study. Mason[8] recently reported 103 cases during the years 1929 to 1934 in children with an average stay in the hospital of 50 days after an average period of 23 days' illness before admission. Graham,[9] with preliminary aspiration during the formative period of the empyema followed by open drainage usually by rib resection, reported an average convalescent period of 38 days in 117 patients treated during the years 1925 to 1931. These figures are certainly better than any obtained by closed drainage during comparable years.

The surgical indications in the treatment of empyema are manifestly first to drain the cavity and empty it, and secondly to obliterate the cavity. Since the convalescent period after open drainage remains long, it seemed that hastening the obliteration of the cavity would be the only available means for shortening convalescence. In the past very little has been done to actively hasten the obliteration of the empyema cavity. The measures employed consisted of deep breathing exercises, blowing colored liquids from one Wolff bottle into another, blowing up balloons or other variations of the same idea, all tending to produce forced respiratory movement. The basis for these procedures has been the belief that the increased excursion of the chest wall

TABLE I

CASES IN CHILDREN

Adm. No.	Adm. Date	Age	Sex	Onset of Pneumonia	First Sign of Fluid	Intercostal Chest Drainage	Type of Pneumococcus	Days of Temperature	Dates Pneumothorax	Actual Days of Drainage	Complete Healing in	Comment
21101	2/19/34	3	M	2/16/34 Left	2/24/34	3/ 3/34	# 3	20 days	3/ 8–150 cc. 3/10–150 cc. 3/12–150 cc. 3/23–250 cc. 3/27–400 cc. 4/ 1–350 cc.	23 days	30 days	After the third air injection, treatment was discontinued because of objection by family physician, but when fever continued unabated, he allowed us to continue the treatment; there was a lapse of treatment for about 11 days.
21195	3/ 2/34	5	M	2/20/34 Right	3/ 8/34	3/17/34	# 2	7 days	3/18–200 cc. 3/20–150 cc. 3/22–150 cc. 3/27–300 cc.	11 days	19 days	Patient developed subcutaneous emphysema of left chest wall on 3/21/34, which completely disappeared on 3/25/34; during the administration of the pneumothorax there was marked increase of drainage from the intercostal drainage tube.
21244 1st adm.	3/ 7/34	12	F	2/25/34 Left	3/ 4/34	3/12/34	# 1	3 days	3/12–250 cc. 3/14–275 cc. 3/18–300 cc. 3/22–250 cc.	4 days	13 days	Roentgen examination of the chest before discharge showed an almost completely expanded left lung with some thickened pleura; against advice, parents signed release and took child home.
21406 2nd adm.	4/ 2/34	12	F	2/25/34 Left	3/ 4/34	4/ 2/34	# 1	6 days	4/ 3–250 cc. 4/ 7–450 cc. 4/12–400 cc. 4/19–400 cc. 4/25–500 cc.	16 days	18 days	Patient was readmitted with history that she developed a sore throat the same day she left the hospital and that night had a slight chill; drainage practically ceased on the fourth day except for a few flakes, which appeared to be washings from a thickened pleura.
21400	3/22/34	5	F	3/12/34 Left	3/24/34	4/ 3/34	# 1	28 days	4/ 4–250 cc. 4/ 7–400 cc. 4/13–300 cc. 4/20–400 cc. 4/26–400 cc.	17 days	21 days	Patient pulled out tube on four different occasions; temperature continued to fluctuate moderately for 11 days after drainage ceased from empyema cavity because of the development of a bilateral suppurative otitis media and follicular tonsillitis.
21548	4/ 8/34	3½	F	4/ 1/34 Left	4/ 7/34	4/ 9/34	# 1	14 days	4/13–150 cc. 4/17–250 cc. 4/21–350 cc. 4/26–400 cc. 4/30–350 cc.	20 days	22 days	Patient developed subcutaneous emphysema on right side on 4/18/34, which disappeared completely on 4/21/34; under the fluoroscope the mediastinum was seen to shift to the left while the pneumothorax was being administered on the right side; there was marked increase of discharge through the intercostal tube during this period.
21771	4/27/34	2½	M	4/13/34 Left	4/20/34	4/28/34	# 3	8 days	5/ 1–250 cc. 5/ 3–250 cc. 5/10–350 cc.	10 days	15 days	There was a rise of temperature on the seventh day, which appeared to be due to some encapsulation as seen by the roentgen rays; 12 hours after the administration of air to the right side the temperature dropped to normal and remained so; there was also a marked increase in drainage.
22147	6/ 1/34	4½	M	5/ 4/34 Right	5/24/34	6/ 4/34	# 4	10 days	6/ 6–200 cc. 6/ 8–350 cc. 6/10–300 cc. 6/12–600 cc. 6/18–500 cc.	14 days	17 days	After injection of 600 cc. of air into the left pleural cavity, causing an almost complete collapse of the left lung, there was no discomfort present but great increase in drainage.

22410	6/24/34	6	F	6/ 3/34 Left	6/24/34	7/ 9/34	# 3	6 days	7/10–250 cc. 7/12–350 cc. 7/14–500 cc. 7/16–400 cc.	9 days	15 days
22812	8/ 3/34	6	M	8/ 1/34 Left	8/ 9/34	8/24/34	# 3	11 days	8/27–250 cc. 8/29–500 cc. 9/ 6–500 cc.	14 days	17 days
24800	2/27/35	9	M	2/25/35 Right	3/10/35	3/20/35	# 2	16 days	3/22–300 cc. 3/25–450 cc. 4/ 1–550 cc. 4/ 4–500 cc.	16 days	20 days
24956	3/14/35	5	M	3/10/35 Right	3/15/35	3/23/35	# 4	12 days	3/26–300 cc. 3/29–400 cc. 4/ 4–450 cc.	14 days	21 days
25363	4/25/35	5	M	4/ 7/35 Right	4/15/35	5/ 1/35	# 3	12 days	5/ 2–300 cc. 5/ 6–400 cc. 5/10–400 cc.	12 days	18 days
25854	6/ 5/35	3½	M	5/15/35 Right	5/21/35	6/ 6/35	# 3	14 days	6/ 8–300 cc. 6/11–350 cc. 6/15–350 cc. 6/20–350 cc.	14 days	22 days
58279	6/ 7/35	4½	F	5/20/35 Right	5/26/35	6/ 8/35	# 3	15 days	6/10–250 cc. 6/12–250 cc. 6/16–350 cc. 6/21–350 cc.	16 days	21 days
27562	11/28/35	5½	F	11/22/35 Right	11/26/35	12/13/35	# 4	5 days	12/15–300 cc. 12/18–375 cc. 12/23–400 cc.	14 days	21 days
28009	1/18/36	4	M	12/16/35 Right	12/23/35	1/20/36	# 2	4 days	1/23–250 cc. 1/26–400 cc. 1/31–400 cc.	14 days	21 days
28691	3/26/36	2	F	3/ 5/36 Right	3/16/36	3/28/36	# 4	5 days	3/30–250 cc. 4/ 2–275 cc. 4/ 7–300 cc. 4/13–300 cc.	15 days	21 days

Uneventful recovery; no respiratory embarrassment in spite of massive collapse of right lung.

Uneventful recovery. Marked increase of drainage after each pneumothorax. No respiratory embarrassment in spite of marked collapse of right lung.

Patient developed a right otitis media on fifth day which ruptured and drained spontaneously Recovery uneventful otherwise.

Patient developed a right lobar pneumonia four days after tonsillectomy and adenoidectomy. Uneventful recovery. On 3/29/35 there was a rise in temperature to 103° F. which was thought to be due to pocketing, but immediately after pneumothorax with subsequent marked drainage temperature fell to 99° F.

Uneventful recovery. No respiratory embarrassment in spite of marked collapse of right lung. Slight subcutaneous emphysema of left chest for three days following first pneumothorax.

On 6/18/ patient had spontaneous drainage from right middle ear abscess. This condition probably prolonged the temperature. Two days later temperature was normal and remained so. Remainder of convalescence uneventful.

On 6/18 patient developed a right otitis media which subsided and then recurred again on 6/21. On 6/23 the ear drained spontaneously and temperature remained down. Convalescence uneventful otherwise.

On admission patient had bilateral pneumonic process with an early right pyopneumothorax. By the time the intercostal drainage was instituted the left side had resolved completely. Following the last pneumothorax, roentgen ray revealed an almost complete collapse of left lung and yet there was no respiratory embarrassment.

Uneventful recovery. The day following the first pneumothorax, the temperature was 99° F. and continued so. Roentgen ray before and after the first pneumothorax showed the lung on the diseased side expanded about three-quarters of an inch so that it was about one-half inch from the chest wall.

Temperature began to drop after first pneumothorax and in three days was normal and remained so. Tube was left in for six days after drainage ceased because visualization of the abscess cavity by means of NaBr solution still showed a 10 cc. cavity which disappeared on twentieth day.

Average days of temperature..... 11 days
Average days of actual drainage..... 14 days
Average days of complete healing.... 19.5 days

TABLE II

CASES IN ADULTS

Adm. No.	Adm. Date	Age	Sex	Onset of Pneumonia	First Sign of Fluid	Intercostal Chest Drainage	Type of Pneumococcus	Days of Temperature	Dates of Pneumothorax	Days of Actual Drainage	Complete Healing in	Comment
21954	5/14/34	26	M	4/24/34 Left	5/15/34	6/ 6/34	# 4	10 days	6/13–450 cc. 6/16–600 cc. 6/19–700 cc. 6/26–500 cc.	21 days	24 days	The first pneumothorax was given one week after the institution of intercostal drainage due to the poor condition of the patient, but following pneumothorax treatment, rapid and uneventful recovery occurred.
22006	5/19/34	42	M	5/ 9/34 Left	5/18/34	6/ 7/34	# 3	19 days	6/13–400 cc. 6/15–600 cc. 6/19–600 cc. 6/25–600 cc. 7/ 1–500 cc.	26 days	29 days	A complicating infection of the chest wall near the drain site continued the temperature for at least a week longer than usual, but after incision and drainage of this area, the temperature stayed down.
22435	6/27/34	54	M	5/28/34 Left	6/20/34	6/30/34	# 3	12 days	7/ 6–600 cc. 7/ 9–700 cc. 7/14–650 cc. 7/19–700 cc.	20 days	24 days	Uneventful recovery. In spite of the age of the patient and relatively fixed thoracic bony cage there was an increase of drainage immediately after each pneumothorax.
28613	3/18/36	28	M	3/ 4/36 Left	4/ 1/36	4/13/36	# 5	11 days	4/15–500 cc. 4/18–700 cc. 4/22–700 cc. 4/27–700 cc. 5/ 3–750 cc.	18 days	25 days	Uneventful recovery except for a carbuncle of the chest wall about one inch from the drain site. In two weeks the lung on the affected side was about seven-eighths expanded. Tube was kept in one week after all drainage had ceased because there was a small area of collapsed lung at left costophrenic angle which subsequently expanded with further contralateral pneumothorax.

Average days of temperature..... 13 days
Average days of actual drainage..... 21.2 days
Average days of complete healing.... 25.5 days

particularly on the affected side rhythmically provides an increased negative pressure within the thorax which supplies the mechanism necessary to produce expansion of the elastic lung. Manifestly, however, even in the most coöperative patients it is impossible to secure whatever benefits may be derived from such respiratory exercises for any considerable portion of the 24 hours in each day. It is probably this very factor which has thrown the Wolff bottles into disrepute with many surgeons.

It was formerly believed that there were only two ways in which a lung collapsed by empyema could expand. One was by the creation of a negative pressure in the pleural cavity, either through the absorption of the air or gasses within the pleural cavity by the surrounding blood vessels or by the rhythmic excursion of the diaphragm and chest wall which produced rhythmic decreases in the intrapleural pressure. The other was by the gradual extension of a connecting granulation tissue between the parietal and visceral layers of the pleura surrounding the abscess cavity in such a manner that the lung is pulled up against the chest wall. It has been stated that this latter method is the only method by which an empyema becomes obliterated and that increased respiratory movement has no effect whatsoever, nor has increased intrapulmonic pressure or diminished intrapleural pressure any effect.[10] This is in all likelihood not true. *A lung collapsed by artificial pneumothorax, expands (slowly if the air is absorbed or more rapidly if the air is drawn off by aspiration) without any connecting granulation tissue between the two layers of pleura, simply as a result of the reëstablishment of negative pleural pressure following respiratory movement.* We have found that there is a rhythmic fall and rise of pressure in the empyema cavity coincident with inspiration and expiration and that the lung can actually be felt to expand with each inspiration.

In a preliminary report[11] we presented a new method of treatment for empyema consisting of closed drainage and contralateral pneumothorax with a view to diminishing convalescence. This method of treatment followed the observation (noted also by others) that in a case of bilateral empyema, drainage instituted on one side resulted in clearance of suppuration in seven days. It seemed as though compression of the lung by the effusion on the untreated side resulted in the more rapid expansion of the lung on the side on which drainage had been established. From this, the idea was born that obliteration of the cavity in a unilateral process might be accelerated by producing the condition of compression of the other lung by artificial pneumothorax.

This procedure has been employed by us in the 21 cases up to the present time. Seventeen of these were children up to the age of 12 and four were adults. The salient features of the cases are shown in Tables I and II.

PROCEDURE.—*Drainage:* From seven to ten days after the termination of the active pneumonic process, closed intercostal drainage is instituted, until which time no diagnostic punctures are made. The chest wall is prepared with iodine and alcohol in the region of a point judged to be the most dependent portion of the cavity (usually in the posterior axillary line). After infiltration of the chest wall with 1 per cent procaine hydrochloride, a small incision is made

with a scalpel, and a trocar and cannula (No. 26 French) is plunged into the cavity. The trocar is removed, and a catheter, previously prepared and clamped at one end, is pushed through the cannula into the cavity. The cannula is then removed and a rubber diaphragm cap is passed over the tube down to the chest wall. This cap is then sealed to the chest wall with collodion or rubber

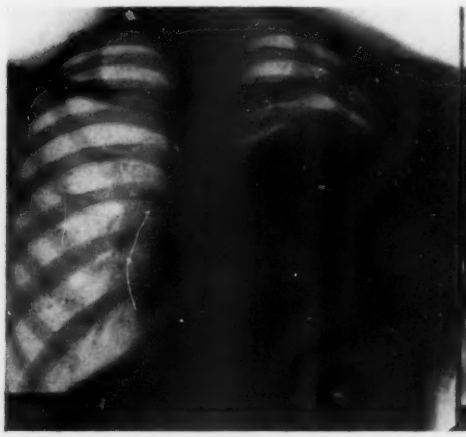

FIG. 1.—(Case 8.) Empyema before intercostal drainage.

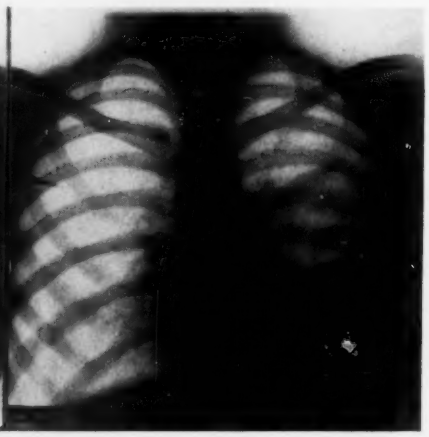

FIG. 2.—(Case 8.) Three days after intercostal drainage and two days after the first pneumothorax.

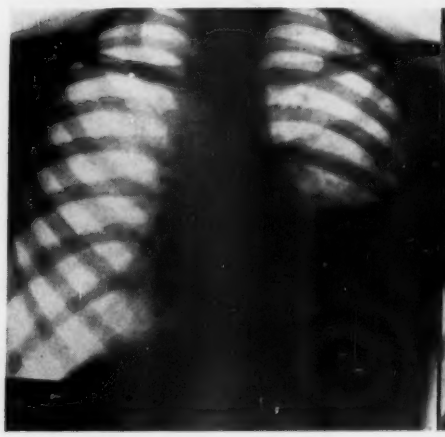

FIG. 3.—(Case 8.) Six days after intercostal drainage.

FIG. 4.—(Case 8). Eight days after intercostal drainage; massive collapse of lung following fourth pneumothorax.

cement and reinforced with adhesive strapping. The catheter is also strapped securely to the chest wall and subaqueous drainage is provided for with a T tube, one end of which is connected to a reservoir containing 1 per cent surgical solution of chlorinated soda. Beginning on the second or third day, the empyema cavity is irrigated with the above solution every three hours night and day.

Obliterating the Cavity.—From two to three days after drainage is begun, artificial pneumothorax is instituted on the unaffected side of the chest. After proper preparation, the skin and subcutaneous tissues in the sixth interspace in the midaxillary line are infiltrated with procaine and the pneumothorax needle introduced into the pleural cavity. Air is then injected, 50 cc. at a time, and the intrapleural pressure is noted. We never give more than 250 cc. to children at the first injection, nor do we ever allow the positive pressure to exceed 3 cm. of water at any time. The needle is then quickly withdrawn, the index finger is applied over the puncture wound and it is sealed with cotton and collodion. In 48 hours another 250 to 400 cc. are administered. Pneumothorax is maintained by successive injections with roentgenographic and fluoroscopic control as the guide until drainage has ceased, the lung is expanded and the empyema cavity is obliterated (Figs. 1 to 5).

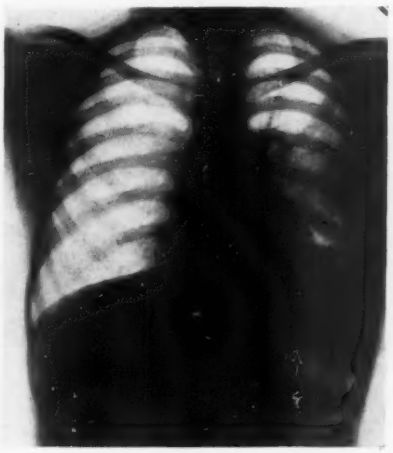

FIG. 5.—(Case 8.) Empyema side almost clear and lung completely expanded 12 days after intercostal drainage was established. There was no drainage for the last three days. Pneumothorax still visible.

OBSERVATIONS.—Immediately after the administration of the pneumothorax the patient began to breathe more rapidly and more deeply. The increase in amplitude of respiration was especially noticeable on the side of the empyema. A short time after this a copious purulent discharge from the drainage tube was frequently noted. In a few cases in which the tube was clamped off during administration of the pneumothorax, pus was forced out of the empyema cavity between the tube and the chest wall, which had previously been air tight. In most cases the increase in rate and depth of respiratory movements was unattended by any subjective respiratory distress. In one instance there was moderate dyspnea and this was accompanied by a forceful ejection of pus from the empyema cavity. Two children complained of slight pain in the chest and shoulder for three or four minutes following the administration of pneumothorax.

Following the introduction of the artificial pneumothorax in these cases, the clinical appearance of the patient became markedly improved. The temperature fell very rapidly, so that the average duration of fever in the uncomplicated cases was less than seven days. Case 5 was complicated with a suppurative otitis media and the duration of the fever was 28 days. Drainage from the empyema cavity ceased on the seventeenth day. Cases 10, 13 and 14 also developed otitis which ruptured spontaneously.

More significant, perhaps, the temperature remained down and it did not show the periods of remission that are so characteristic of empyemata treated

by other methods. "Pocketing" was noted only once. This was is Case 7. In this instance drainage had suddenly ceased, but the temperature and pulse remained elevated. A refill with 600 cc. on the contralateral side, causing an almost complete collapse of the sound lung, produced a copious discharge with an immediate subsidence of temperature elevation. Here the pneumothorax apparently interfered with an obliterated "pocket" in the process of formation. In Case 11, the rise in temperature to 103° on the third day after the first pneumothorax might have been due to "pocketing" because a second pneumothorax on that day was followed by a profuse discharge and subsidence of fever. The appetite improved very quickly and the children gained weight rapidly. By the fourth day after the introduction of the first artificial pneumothorax, most of the pus had been evacuated from the chest. There was very little drainage at that time and the cavity rapidly became smaller as the lung rapidly expanded. Between the seventh and the tenth day after the introduction of the first artificial pneumothorax, the cavity was usually too small to contain 25 cc. of surgical solution of chlorinated soda. The average period, until there was no more drainage of pus in children, was 14 days after the thoracotomy. The obliteration of the cavity is demonstrated by comparisons of roentgenograms taken before and after the introduction of the artificial pneumothorax. The only simple complications in this series were subcutaneous emphysema in three cases on the side of the emphyema, which disappeared in from two to four days and a chest wall infection near the drain site in Case 14.

In the adults the average duration of drainage was 21.2 days and the average duration from the institution of drainage to healing was 25.5 days. The average duration of healing for the 21 cases of adults and children was 20.6 days. That this method is not completely devoid of danger is shown by the following two cases.

Case 1.—A male child (No. 25909), one year of age who, previous to his admission to the hospital, was sick for eight days with a high temperature and an upper respiratory infection. After four days of illness the baby developed well marked signs of pneumonia in the left side of the chest. At the time of admission, which was on June 11, the general condition of the child was noted as being improved, respirations were less labored, the abdomen was slightly distended, the liver was palpable one and one-half fingers' breadth below the costal margin. There was flatness over the entire left side of the chest which diminished breathing in the axilla, bronchial breathing in the middle third of the chest posterially. The impression was that there was a pleural effusion. Roentgenologic examination revealed a dense opacity occupying the lower two-thirds of the left chest with a characteristic fluid level. The child improved clinically until on the eighteenth it was decided that aspiration should be attempted, at which time pus was obtained showing pneumococci. On the twenty-first an intercostal drainage was performed according to the technic described, and continued until the twenty-third when at 10 A.M. 100 cc. of air were given for the initial pneumothorax. The child bore the introduction of the air very well. At three minutes after 12, when the nurse set the child up to feed it, the child became cyanotic and gasped for air. The head was lowered, stimulation was administered and oxygen and carbon dioxide inhalations were given but without avail, and the child expired in 17 minutes. A heart puncture with a 50 cc. syringe and a long needle was made. As soon as the needle entered the cardiac cavity, the plunger was forced upward

by blood and gas bubbles intimately admixed. The appearance was similar to bubbling vichy water. It was felt that the fatal outcome was the result of a delayed air embolism attendant upon a pneumothorax.

Case 2.—(No. 28296.) A girl of 12 whose onset of pneumonia occurred February 3, 1936. Seven days later the clinical signs of fluid on the left side developed. The child was admitted to the hospital February 21, and intercostal drainage established on the twenty-fourth. The culture showed a large number of hemolytic Streptococci and a few pneumococci. A contralateral pneumothorax was established February 27, 1936, 300 cc. of air being introduced slowly so that the final intrapleural pressure in the right hemithorax was —2. The following morning at 3 A.M. the patient suddenly became dyspneic and then cyanotic. The right side of the chest was markedly tympanitic and no breath sounds could be heard at all. The pulse became very rapid, and it was apparent that a rightsided tension-pneumothorax was developing to such proportions as to seriously threaten life. Air was removed from the right side of the chest by aspiration with a large syringe and the symptoms subsided for a few hours, only to redevelop. After several such aspirations in the following 12 hours with only a brief transitory relief after each, a small catheter was inserted through a trocar stab (closed method) and continuous suction maintained with very low pressure by means of a vacuum pump. The lung expanded fully in six hours, the clinical improvement coinciding with the expansion, and the dyspnea and cyanosis disappeared. Three days later the tube was removed and no further clinical difficulty from tension-pneumothorax resulted and the patient convalesced uneventfully. Apparently the complication resulted from an injury to the lung by the needle used in inducing the therapeutic pneumothorax. This injury produced a communication between the bronchopulmonary tree and the pleural space so that with each respiratory movement of the ribs and diaphragm, as air rushed into the tree it gained entrance into the pleural space where it was trapped. Each inspiratory movement brought more air which in turn produced more collapse of the right lung so that ultimately insufficient aeration and anoxemia resulted. Unquestionably, death would have resulted if the tension-pneumothorax had not been relieved. The complication yielded rapidly to treatment, however, and the hole in the lung was sealed over very quickly. No further pneumothorax therapy was tried in this case because it was believed that difficulty might be encountered as a result of inflammatory changes in the visceral and parietal layers of the pleura at the site of injury.

The amount of air injected into the contralateral pleural space at each pneumothorax is indicated on the hospital chart. The interpretation of the figures is of course dependent upon the size of the chest and the total lung volume. The relation between the amount of air injected and the previous total lung volume was not determinable, but an approximation could be obtained by roughly comparing the injected volume to the volume of the unaffected lung as their areas appeared on the roentgenograms. The method employed by us consists of making a tracing of the area occupied by the lung after pneumothorax collapse and another of the total area of collapsed lung plus injected air, using a roentgenogram obtained immediately after the pneumothorax induction. The two tracings are made on the same kind of paper and then they are cut out and weighed. The weight of the tracing of the collapsed lung divided by the weight of the other (total of collapsed lung plus air) gives an approximate percentage of lung left after collapse. In the children studied the average injection of 250 cc. resulted in reducing the area of the functioning lung to about 40 per cent.

Where the injection of air is made in greater amounts or on top of already

existing partial collapse, it is possible to reduce the size of available lung to as little as 27 per cent using this method of estimation (Fig. 6).

There are drawbacks to the use of this method for diminishing the convalescent period. One of the outstanding features in favor of rib resection and tube drainage (in contrast to all other methods) was the small amount of care the patient needed subsequently. The tube was left in until the cavity obliterated itself. An occasional roentgenogram showed the progress of the case. With contralateral pneumothorax and closed drainage, however, many

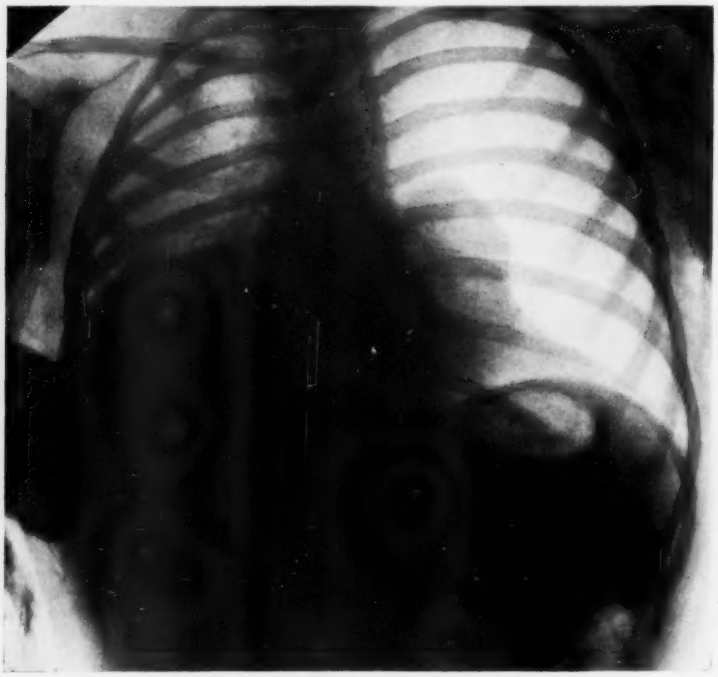

FIG. 6.—(Case 17.) Massive collapse of contralateral lung by pneumothorax so that its function is reduced to 27 per cent.

additional elements in the care of the patient are added. In the first place, the induction of the pneumothorax necessitates time and also additional care. Roentgenograms are necessary before and after the pneumothorax. In our series the average number of roentgenograms for each case was 12.2. It must be apparent that patients so treated require a much greater amount of work in taking care of them. However, that should not be a deterrent if the convalescence is hastened.

It seems quite likely that convalescence might be still further hastened. Since the method was (and still is) in the experimental state, in many instances the tube was allowed to remain in situ several days longer than it was believed to be needed to insure against too early removal with recurrence, there being no accurate criteria for the determination of when the cavities were both sterile and obliterated. It is believed that these will shortly be available.

MECHANISM.—One of the diagnostic roentgenographic signs of fluid in a pleural cavity is the displacement from the median line of the trachea and mediastinal contents towards the unaffected side. When free drainage of any kind is established there is a gradual return towards the median line of the displaced organs. However, examination of the roentgenograms following the induction of the artificial pneumothorax reveals the fact that the trachea and the mediastinal contents are pushed over toward the side with the empyema. Accompanying this shift there is a coincident marked increase in the discharge from the empyema cavity through the tube which results from the increase in pressure within the empyema cavity, a pressure sufficient to force pus out around an otherwise air and liquid tight tube, if the tube is clamped during the pneumothorax administration. This can only be interpreted as meaning that there is a compression of the empyema cavity by the shift of mediastinal and thoracic contents resulting from the induction of the artificial pneumothorax.

It has long been known that the induction of an artificial pneumothorax is not followed by any change in the tidal air.[12, 13] This is so because the unaffected side compensates. We have found that even in cases of empyema, tidal air is not diminished by producing a pneumothorax artificially on the side opposite the emypema. In our previous report[11] we presented a graph demonstrating the marked increase in respiratory pressure variations in the empyema cavity coincident with the contralateral pneumothorax induction. This was accompanied by an increase in the number of respirations per minute, thus also increasing the total ventilation of the lungs.

This suggests the explanation for the absence of subjective dyspnea in our cases when the pneumothorax is induced. It also suggests the reasons for the absence of cyanosis despite massive collapse of the contralateral lung.

Thus the influence of a contralateral pneumothorax on the obliteration of the empyema cavity is both a direct and indirect one. The former is due to transmission of pressure from the pneumothorax through the mediastinum and pulmonary tissues to and upon the empyema cavity, compressing it. The latter is related to a much more complicated mechanism designed apparently to maintain adequate pulmonary ventilation despite handicapping complications. This mechanism is able to maintain the normal level of tidal air after the complete collapse of one lung by pneumothorax.

SUMMARY.—(1) We have reported 118 cases of acute empyema treated by open drainage after rib resection, 113 of which healed in 45 days from the day of drainage.

(2) Twenty-one additional cases treated by closed drainage and contralateral pneumothorax were presented, which showed a lapse of 20.6 days between the institution of drainage and complete wound healing.

(3) The methods by which obliteration of the empyema cavity may be favored were discussed.

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THE TREATMENT OF EMPYEMA

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IN SPITE of the work of the Empyema Commission,[2] which did much to clarify the ideas regarding the pathologic physiology and dangers of certain forms of treatment of empyema, there still exists a wide diversity of opinion concerning methods of effecting a cure. This is probably due to efforts to apply one method of treatment to all cases regardless of the stage of the disease or the type of organism involved.

It would seem that this is no longer excusable. The report of the Empyema Commission, substantiated by the work of Graham[1] and of Graham and Bell,[3] has set forth clearly the fundamental principles that must be followed. Actually, there is no justification for the many arguments one may hear or read as to whether there shall be open or closed drainage. The important thing is the following of the principles: (1) Avoidance of an open pneumothorax in the acute stage of the disease; (2) prevention of chronic empyema by the sterilization and obliteration of the empyema cavity; and, (3) provision of supportive measures to raise the resistance of the patient.

There has been something of value in most of the methods of treatment advocated. The objectionable feature has been the feeling of some authors, that their particular method should be applied to all types of empyema and carried through to a final conclusion. It seems unbelievable that anyone should advocate for all cases: (1) Aspiration alone; (2) intercostal tube drainage alone; (3) rib resection with open drainage alone.

Almost any method of treatment, provided it is within the realm of reason and common sense, can be made to work provided enough attention is given to it. As an example, there is no doubt at all that some cases of empyema can be cured by repeated aspirations. Every one who treats empyema, however, must have encountered those cases, particularly those caused by the pneumococcus, in which the pus has become so thick and masses of coagulated fibrin so large and tenacious as to make aspiration absolutely impossible, even with the largest of aspirating needles.

In relying upon the intercostal drainage tube, the tendency may be to wait too long after improvement has reached a standstill before resorting to other measures. Even with a fairly large tube, adequate drainage cannot always be effected, especially where large masses of fibrin are forming in the empyema cavity. As the pus becomes thicker there may be additional pockets formed which are not drained by the intercostal tube.

Penberthy and Benson[5] have shown, however, that this method may give good results with a large series of cases in children, extending over a long

period of time. Use of any method over a long period of years will, of course, largely eliminate the variability in results which might occur due to difference in bacterial virulence.

If one were forced to choose one method for the treatment of empyema and use it alone, probably the safest and most efficacious would be the resection of a portion of a rib with open drainage. With this method, however, must be exercised the judgment as to the proper time to operate. Open drainage too early in the illness, especially with the Streptococcus empyema, may result in early death, as occurred in the army camps during the influenza epidemics.

There is a difference of opinion as to the influence of different types of treatment on duration of illness and different series of cases could be used to prove different points. While the length of illness is important, it is not of prime importance. Another factor worthy of some consideration is the comfort of the patient during the period of drainage. With the open method, dressing must be carried out frequently.

A safe method is to adopt first the three principles promulgated by the Empyema Commission as a guide for whatever form of treatment is used. The advantages of the three methods discussed above may be utilized and their objectionable features may be avoided. Aspiration certainly has its place and should always be used: (1) To determine the type of organism present; (2) to reduce the toxicity during the formative stage of the disease; and, (3) in some instances to avoid for a time any other procedure which might put an additional burden on a patient seriously ill. Once the pus has become thick, an intercostal tube may be inserted and through this aspirations and irrigations, if desired, may be carried out. If progress ceases with this second stage of the treatment, one should consider that additional pockets may be undrained or that the character of the pus is making the tube aspiration or irrigation unsuccessful.

Once this stage is reached, resection of a portion of a rib is indicated. By this time the formative stage of the disease will have passed and there will probably be an adequate stability of the mediastinum. Opening the chest will permit the removal either with forceps or a suction tube the masses of coagulated fibrin which prevent clearing of the infection. It will also be possible to break down trabeculae which may have formed and to open pockets which are draining inadequately or not at all. Further handling of the wound is a matter of judgment for the operator. Many patients will do better by leaving the wound open. Some will do well by placing a large drainage tube in the wound. In some instances the period of illness will be shortened and a satisfactory result obtained by introducing a tube into the empyema cavity through a stab wound, the operative wound being tightly closed, a reconversion to closed drainage. When this is done it may be wise to use a small rubber subcutaneous drain. A large percentage of such wounds will heal per primum.

There need be no quarrel as to the type of irrigating solution used. The

important thing is to have adequate drainage. There are those of us who still feel that Dakin's solution is of value for its antiseptic properties and as an aid in dissolving the fibrinous wall of the empyema cavity. One cannot be certain, however, that its most important function is not the mechanical washing out of the cavity.

No method of treatment can be adopted and be expected, after a given length of time, to have effected a cure. Empyema is a variable disease and whatever method of treatment is used, it must be under careful and constant supervision. It should be needless to say that that which might increase embarrassment of physiologic processes should be avoided.

There have been proposed in the past, procedures whose proponents claimed fulfilled the requirements of the principles of adequate treatment but which after careful study would seem to include that which was embarrassing, rather than helpful, to a restoration of normal physiology. In 1935, Koster[4] and his coworkers proposed the use of pneumothorax on the unaffected side in the treatment of empyema. Better drainage and a shorter period of illness were reported from a series of eight cases. Progress roentgenograms were said to show a mediastinal shift to the empyema side. The reported improvement was thought to be the result of increased respiratory effort on the empyema side and to the mediastinal shift. While there is normally a great difference between tidal air and vital capacity it would seem that the reduction in the vital capacity which would occur following the pneumothorax is not in any way justifiable in a patient already acutely ill.

The increased rate and depth of respiratory effort on the empyema side would seem to be evidence of unjustified embarrassment rather than an exhibition of a curative process. It hardly seems reasonable to bring about labored respirations in a lung recently diseased with pneumonia.

This type of treatment could have no effect other than that which results from the loss of function of the compressed lung, except that which might result from mediastinal shift. To deliberately produce this with its possible attendant respiratory and circulatory embarrassments would seem to be unjustifiable. If the vital capacity is impaired by reduced function of one lung by disease, no possible handicaps should be placed in the way of normal functioning of the other.

CONCLUSIONS

(1) The valuable features of aspiration, closed drainage and open drainage may all be utilized, if necessary, in their turn.

(2) Every case of empyema must be carefully treated and the greatest judgment exercised in order to avoid continuing too long with one method of treatment, if improvement is not occurring.

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CARCINOMA OF THE AMPULLA OF VATER

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IN THE group of diseases causing obstructive jaundice, carcinoma of the ampulla of Vater stands out as a rather rare but distinct clinical entity. The distinctiveness of the disease is emphasized by the similar clinical picture presented in the individual cases. For the purpose of clarifying the clinical picture and the diagnosis of carcinoma of the ampulla of Vater, the subject is herein reviewed, and 14 authenticated instances of this disease which have been observed in the New York Hospital between 1915 and 1935 are added to the literature. The first treatise on carcinoma of the ampulla of Vater is that of Busson,[1] published in 1890. From the literature on obstructive jaundice and carcinoma of the duodenum, he collected 11 cases of ampullary carcinoma. In the next decade there were many contributions, notably that of Hanot,[2] in 1896. In the same year his pupil, Vincent Georges,[3] was able to collect 20 cases. But it was not until Halsted[4] successfully resected an ampullary carcinoma in 1898 that the subject attracted wide attention, chiefly in the form of isolated case reports. In 1901 Schüller[5] collected 41 cases, and in 1913 Outerbridge[6] published an extensive report on 110 collected cases. No one since Outerbridge[6] has attempted to collect all the reported cases, most authors confining their attention to the cases treated surgically. In 1927, Cohen and Colp[7] collected 59 cases treated by resection of the tumor. The most recent study is that of Hunt and Budd[8] who, in 1935, collected 76 cases that were treated surgically.

Incidence.—The incidence of carcinoma of the ampulla of Vater is best shown by large autopsy series. In Kellogg's[9] statistics on 151,784 autopsies, there were 50 or 0.03 per cent carcinomata of the duodenum. According to the combined statistics of Rolleston,[10] Geiser[11] and Fenwick,[12] 66 per cent of duodenal carcinomata are peri-ampullary; this would indicate that about 0.02 per cent of all autopsies show peri-ampullary carcinomata of the duodenum. As approximately half of the cases of ampullary tumor have their origin in the duodenal papilla, the true incidence of carcinoma of the ampulla of Vater, in the sense in which the term is used in this study, is about 0.04 per cent. In the New York Hospital series, seven of the 14 cases were autopsy cases, occurring in 3,000 autopsies, an autopsy incidence of 0.2 per cent. This figure is unquestionably high.

Age Incidence.—There is nothing distinctive about the age incidence of carcinoma of the ampulla of Vater. Like all cancer, it is more common in older people. The average age in Rolleston's 23 cases is 55.2 years, in Outer-

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bridge's 110 cases, 54.6 years. The youngest case on record is one of Mayo-Robson's,[13] a male aged 30. Rolleston mentions a case 81 years old. The average age in this series is 49.3 years; the youngest 38, the oldest 59 years.

Sex Distribution.—Carcinoma of the ampulla of Vater is more common in men than in women, the ratio being roughly two to one. Pallin[14] had 12 males to one female, but the preponderance of males in his cases is probably accidental. In this series there were ten males and four females.

ETIOLOGY.—*Relation of Stones.*—Proceeding down the biliary tract from the gallbladder through the common duct to the ampulla of Vater, the frequency of the coincidence of gallstones and cancer decreases. Cholelithiasis is associated with carcinoma of the gallbladder in about 80 per cent of cases and with carcinoma of the common duct in only about 25 to 35 per cent. In carcinoma of the ampulla of Vater the relation is still less striking but quite definite. Gallstones were present in 15 per cent of Schüller's 41 cases, 20 per cent of Outerbridge's 110 and 25 per cent of Pallin's 52 cases. In this group of cases, 22 per cent had cholelithiasis. In most reported series of ampullary carcinoma the incidence of cholelithiasis is about twice the usual 8 to 10 per cent incidence of cholelithiasis in this age group. Like the fundus and neck of the gallbladder, the ampulla of Vater is subjected to greater chronic mechanical irritation by stones than other portions of the biliary tract. This fact is of significance when one considers that 80 per cent of carcinomata of the gallbladder start at the fundus or neck of the organ, those areas most subject to the mechanical irritation of stones. The presumptive evidence certainly favors the view that the passage of biliary calculi predisposes to carcinoma of the ampulla of Vater. Payr,[15] Donati[16] and others feel that stones are formed secondarily to carcinoma, due to biliary stasis. Decidedly against this theory is the fact that biliary calculi are seldom found in carcinoma of the head of the pancreas, a disease in which biliary stasis dominates the clinical picture.

Relation to Ulcers.—The sex distribution of the Vaterian carcinomata seems inconsistent with the rather logical theory of etiology based on chronic irritation due to the passage of gallstones. Whereas cholelithiasis is about seven times as frequent in women as in men, carcinoma of the ampulla of Vater is more common in males, the ratio being roughly two to one. This would not suggest that cholelithiasis fails to be a definite etiologic factor, but that there is an additional factor present in males that is not present in females. It is well known that the formation of ulcers in the first portion of the duodenum is more common in males than in females. It seems reasonable to suggest that similar irritative factors, whatever they may be, also influence the development of Vaterian carcinoma in the second portion of the duodenum. Opposing this view is the fact that duodenal ulcers and carcinoma of the ampulla of Vater seldom coexist. But it is certainly true that individuals, as well as various tissues in the same individual, react in a variety of ways to identical stimuli.

Embryonal Rests.—Another etiologic factor mentioned in the literature

is that of embryonal pancreatic rests. Pic[17] regarded carcinoma of the ampulla of Vater as an aberrant form of pancreatic carcinoma. Whereas aberrent pancreatic rests do occur in and about the second portion of the duodenum, they seldom undergo carcinomatous changes (Branch and Gross).[18] Pic's theory is but rarely applicable.

ANATOMY.—Before considering the disease further, a clear concept must be established of what is meant by tumors of the ampulla of Vater. The literature on the subject is confusing due to the complex and variable anatomy of the distal biliary and pancreatic ducts and their relation to the duodenum.

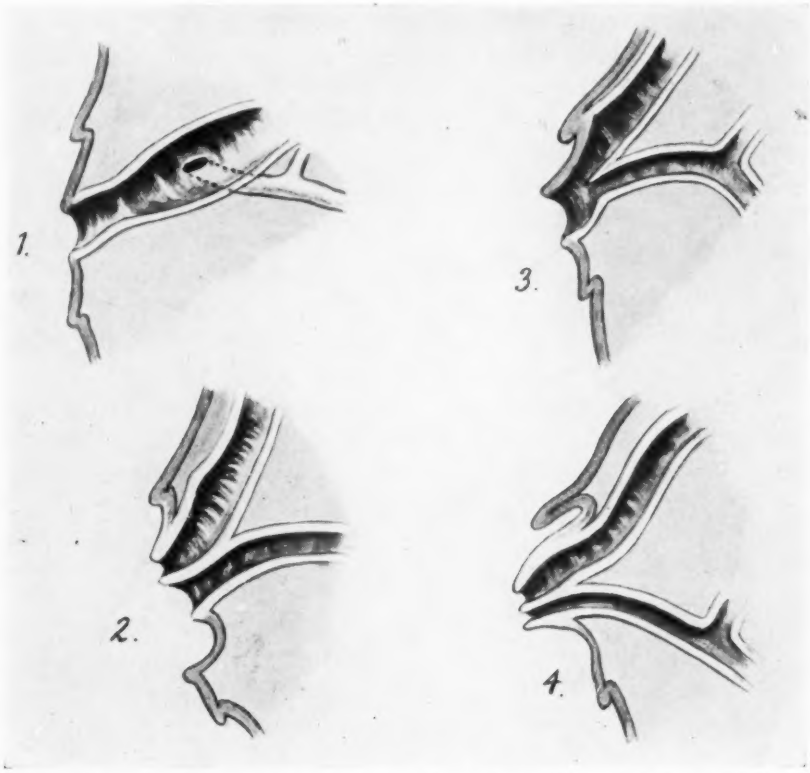

FIG. 1.—Four anatomic types of the ampulla of Vater. Lettule. Nattan-Larriere.[21] (Reprinted from Sweet, J. E.: Surgery of the Pancreas. Internat. Clinics, Series 25, 4, 293–357.)

For this reason Rolleston considers many of Outerbridge's collected cases biliary duct rather than ampullary tumors. Authors have described different diseases under the same title.

Abraham Vater[19] first described the regional anatomy of the ampulla of Vater in 1720. Domenico Santorini[20] described the pancreatic ducts and their outlets in 1775. Vater's name became associated with the ampulla, while the name of Santorini in medical literature applies to the major and minor papillae through which the pancreatic ducts enter the duodenum. Subsequently the regional anatomy has been thoroughly studied by Lettule and Nattan-Larriere,[21] who found four anatomic types (Fig. 1).

Considered academically, a tumor of the ampulla of Vater is one which arises in the ampullary epithelium. If no ampulla exists, such a tumor cannot occur. This restricted concept excludes from discussion all tumors of the terminal biliary and pancreatic ducts and of the duodenal papilla. This entire area, however, is not more than 1 cm. in diameter, and tumors usually involve the entire region, causing indistinguishable clinical and pathologic pictures. Therefore, it seems practical that all tumors of the ampullary region be considered in one clinical group, regardless of their histogenesis.

PATHOLOGY.—*Site of Origin.*—Outerbridge has described six possible histogenetic origins for ampullary tumors. In most instances it is impossible to determine accurately the origin of these tumors, for the entire ampullary region is involved by the growth. Early cases, however, have demonstrated that each of these six tissues may undergo carcinomatous changes.

(1) *Epithelium Lining the Ampulla of Vater* (when an ampulla is present).—Rolleston collected 23 such cases, and a number of cases have been reported since. These tumors are small, for when a tumor of the ampulla attains any size, its exact origin becomes obscure. The majority are adenocarcinomata less than 1 cm. in diameter, though infiltrating sessile ulcerating tumors occur. In Case 8 of this series, the origin of the tumor was quite definitely from the ampullary epithelium.

(2) *Duodenal Epithelium of the Peri-ampullary Region or the Duodenal Papilla.*—This is probably the most common site of origin of carcinoma of the ampullary region, for, roughly, half the cases in the literature arose at this point. Many of these cases, indistinguishable clinically from other ampullary tumors, are reported as carcinoma of the duodenum. Rolleston, Geiser and Fenwick have collected 104 such cases. These tumors are papillary or infiltrating. The infiltrating tumors tend to ulcerate. Ulceration is more common in this position than in any other. The infiltrating tumors involve the duodenal wall and not uncommonly cause an annular constriction of the second portion of the duodenum. The obstruction of the duodenum at the level of the ampulla seen in Cases 1, 3 and 11 suggests that in these cases the tumor originated in the peri-ampullary duodenal epithelium.

(3) *Epithelium of the Terminal Common Duct.*—It is difficult to say just where the line should be drawn between carcinoma of the terminal bile ducts and carcinoma of the ampullary region in the broader sense, for carcinoma may occur at any point along the common duct. Since tumors of the terminal 1 cm. of the common duct are clinically identical with and often grossly indistinguishable from actual ampullary tumors, and since the same operative treatment usually is indicated, it would seem logical to include such tumors in the group under discussion. There are a number of such cases recorded in the literature. They may be papillary or infiltrating. No examples of this tumor were seen in the present series.

(4) *Epithelium of the Terminal Pancreatic Duct.*—Lettule,[22] Carnot and Harvier,[23] and Luzzatto[24] have described tumors arising from the terminal pancreatic ducts. These are rare enough to be considered curiosities, and

must be seen very early to be recognized. None of the present series could be placed in this group.

(5) *Brunner's Glands in the Submucosa of the Papilla.*—Klotz[25] has described a tumor which, because of the microscopic picture, was thought to originate in Brunner's glands. It was an ulcerating, infiltrating adenocarcinoma. No other examples of this tumor are on record.

(6) *Aberrant Pancreatic Tissue.*—Pic and Pilliet[26] and Eloesser[27] have described tumors of the ampullary region which appeared to originate in aberrent pancreatic tissue. The tumor in Case 7 of the present series may well have had its origin in either Brunner's glands or in aberrant pancreatic tissue in the peri-ampullary duodenal wall. Such a theory is, of course, speculative, but there are certain features of the tumor which support this view. The tumor centered in the duodenal wall and appeared to involve the neighboring pancreas secondarily, the duodenal mucosa was intact but infiltrated by tumor, and Brunner's glands in this region were entirely replaced by tumor.

In Cases 2, 4, 5, 6, 9, 10, 13 and 14 of the New York Hospital series the histogenetic origin of the tumors could not be determined. In all of these the entire ampullary region was involved.

Gross Appearance.—Carcinomata of the ampulla of Vater may be divided grossly into (1) papillary and (2) ulcerating tumors with variations between these two extremes. Papillary carcinomata are probably the more common. They project into the lumen of the terminal common duct or ampulla, thereby causing obstruction. If the papillary tendency is marked, the tumor may protrude from the duodenal papilla as a whitish or pinkish polyp, which is quite firm and may be eroded. The size of these tumors varies from a few millimeters to 3 cm. in diameter. Though most of the papillary tumors are less than 1 cm. in diameter, Angeli[28] has reported one the size of an orange. It is difficult to agree with Cohen and Colp's view that tumors protruding from the duodenal papilla invariably arise in the common duct.

The ulcerating carcinomata may be seen as flat, plaque-like tumors, 1 to 3 cm. in diameter, with hard raised edges. By the time these tumors give rise to biliary obstruction, the entire ampullary region is usually involved in a hard, infiltrating, ulcerating, bleeding mass not less than 1 cm. in diameter, easily palpable through the duodenal wall. The bulk of the mass is composed of infiltrating tumor, which causes the obstruction. Occasionally the tumor may ulcerate as fast as it infiltrates, thereby excavating the ampullary region and releasing the biliary obstruction. It is this type of tumor that accounts for the intermittent jaundice occurring in some cases.

At operation the surgeon may have difficulty in localizing the biliary obstruction, particularly if the tumor is a small papillary one with little infiltration at the base. Such a tumor can be felt only by the most careful palpation of the ampullary region. One cannot be certain of an ampullary tumor until the duodenum is opened and the tumor visualized, but the palpation of a hard small mass in the ampulla should arouse suspicion.

Types of Tumor.—There are in the literature a few isolated instances of

benign ampullary tumors. Calzavara[29] and Verhoogen[30] reported benign adenomata, while benign papillomata have been recorded by McPhedran,[31] Stein,[32] and Archibald.[33] A carcinoid growth was reported by Brentano[34] and an adenofibroma by Herrick.[35] Christopher[36] has reviewed these cases and adds one case of a benign adenoma. Since then, Landivar[37] has reported a benign papilloma.

Malignant tumors of this region other than carcinoma are rare. Moll[38] and Dencks[39] recorded spindle cell sarcomata of the ampulla, Duval[40] reported a melanoma, or pigmented papillary adenocarcinoma (Ewing[41]). Sheppard[42] reported this same case. Jones[43] also reported a melanoma, the origin of which was obscure. With these exceptions, all the tumors of the ampullary region reported in the literature have been carcinomata.

Rolleston and Ewing find that ampullary carcinomata are practically always columnar cell. Indeed, one is impressed with this fact in reading over the microscopic reports of the various cases. That other varieties may occur here as elsewhere in the biliary tract, however, is emphasized by Arnsperger's[44] finding a scirrhous carcinoma, Cohen and Colp a squamous cell carcinoma and Walters[45] a colloid carcinoma. Whereas these later types must be rare in the ampullary region, there is little doubt but that all varieties of columnar cell carcinomata exist, from the more benign papillary to the most malignant infiltrating tumors. This is borne out by the fact that some of the papillary carcinomata have been cured by local excision, while others of the infiltrating type have recurred after wide excision.

The columnar cell carcinomata take the form of adenocarcinoma, the cells being arranged in alveoli or pseudo-alveoli. The extent of infiltration is variable, in general being more marked in the flat, ulcerating tumors than in the papillary ones. All of the New York Hospital series were adenocarcinomata. In some, the alveoli were lined by cells that were definitely columnar, but in others anaplasia was so marked that no true columnar cells could be seen. There was wide variation in the desmoplastic reactions in the group. A few tumors had definite scirrhous tendencies. while others were composed of sheets of anaplastic cells with scant intracellular tissue and little tendency to form alveoli.

Efforts have been made to differentiate ampullary tumors and pancreatic tumors, with which they may be confused, by comparing the shape of the epithelial cells. Rolleston states that ampullary tumors are composed of columnar cells, while the cells of the pancreatic tumors are spherical. Ewing, on the contrary, speaks of both ampullary and pancreatic tumors as consisting of columnar cells. Whereas the epithelial cells in a well differentiated ampullary tumor may be taller than those in a similar tumor of pancreatic origin, in our experience this is neither a reliable nor helpful criterion for differentiation. When anaplasia is marked, the epithelial cells of both ampullary and pancreatic tumors may assume bizarre shapes.

Metastases.—The growth characteristics of carcinoma of the ampulla of Vater are similar to those of other tumors of the gastro-intestinal tract, yet

metastases are relatively infrequent. This is not due to any inherent benign quality of the tumor, but due to its strategic location. Biliary obstruction occurs while the tumor is relatively small, and death often supervenes, due to interference with the vital functions of the liver and, possibly, of the pancreas, before extensive growth or metastases occur.

Oehler[46] and Geiser believed the tendency to metastasize great, while Lettule and Kausch[47] and Schüller found metastases rare. Perry and Shaw[48] and Aynaud[49] found metastases in 20 per cent of cases, and Outerbridge in 22 per cent. In the New York Hospital series, five cases or 36 per cent had metastases. In a group of cases in which palliative cholecystogastrostomy or cholecystoduodenostomy had been successfully carried out, it is likely that metastases would be as frequent as in carcinoma of the stomach.

The spread of carcinoma of the ampulla of Vater is accomplished by: (1) Local extension or infiltration; (2) lymphatic metastases; and (3) visceral metastases.

(1) Local Extension: By infiltrating the duodenal papilla and wall, the primary tumor must traverse the intrinsic network of submucosal and subserosal capillary lymphatics, which facilitate its spread. The intrinsic lymphatics allow the tumor to infiltrate the duodenal wall in an annular fashion, thereby causing duodenal obstruction. These intrinsic lymphatics drain into a group of nodes which lie between the second portion of the duodenum and the head of the pancreas, and these nodes in turn receive the lymphatic drainage of the head of the pancreas. Carcinoma of the ampullary region frequently invades the head of the pancreas through this intimate relation of the lymphatics. It shows little tendency to invade the pancreatic acini, but usually infiltrates the areolar tissue between the pancreatic lobules, a feature which may be useful in differentiating the tumor microscopically.

In the New York Hospital series three cases (Cases 1, 3 and 11) had annular infiltration of the duodenal wall. In five instances (Cases 1, 2, 3, 5 and 7) the head of the pancreas was infiltrated. All of these had gross involvement of the pancreatic nodes. In Case 3 there was infiltration of adherent jejunum.

(2) Lymphatic Metastases: The lymph nodes on the surface of the pancreas drain in two directions, (a) into the periportal nodes which run up to the hilum of the liver, and (b) into the pre-aortic nodes. As one might expect, these are the lymph nodes most frequently involved in carcinoma of the ampulla of Vater. Lymphatic metastases beyond these groups of nodes are very rare.

Four of the New York Hospital series (Cases 2, 3, 5 and 7) had metastases to the periportal nodes, while three (Cases 2, 5 and 7) had metastases to the retroperitoneal or pre-aortic nodes. Case 7 was very unusual both clinically and pathologically. Practically all the nodes in the peritoneal cavity, as well as the cervical nodes, were filled with tumor.

(3) Visceral Metastases: These may occur through lymphatics or, as illustrated by Case 3, in which the portal vein was infiltrated by tumor, through

the blood stream. The former route is the more usual in carcinoma of the ampulla of Vater, as in most carcinomata. The liver is the organ most frequently involved, and this probably occurs in a retrograde manner through the periportal lymphatics.

In the New York Hospital series, five cases (Cases 2, 3, 4, 5 and 7) had hepatic metastases. Other organs rarely are involved. Case 7 had metastases in the lung, pleura, peritoneum and omentum, but this is quite unusual.

Pathologic Effects Upon Other Organs.—Obstruction of the biliary and pancreatic ducts at the ampulla of Vater initiates pathologic changes in the liver, pancreas, gallbladder and biliary ducts. These changes are not specific for malignant obstruction at the ampulla, but also occur in obstruction at this point due to stones. Most of the pathology is explained by the simple physics of hydrostatic pressure, though infection occasionally plays a complicating rôle.

The liver is invariably somewhat larger than normal in common duct obstruction. The increase in bulk of the organ is due to two factors: (1) dilatation of the biliary ducts all the way back to the bile capillaries, and (2) increase in the size of the liver cells due to hepatitis. The organ takes on a greenish hue due to its engorgement with bile. In ulcerating ampullary tumors the chances for infection are great, and a suppurative cholangeitis with multiple hepatic abscesses may develop. Such was the condition found at operation in Cases 4 and 9.

The head of the pancreas is frequently nodular and indurated, a finding which may distract the attention of the surgeon from a small ampullary tumor. The pancreatic ducts are often dilated and some degree of chronic interstitial pancreatitis is usually present. This process is the result of obstruction of the pancreatic ducts, and may progress to fibrous atrophy of the glandular elements of the pancreas. Just what rôle obstruction of the pancreatic ducts plays in the clinical picture of ampullary carcinoma is not known. That loss of all pancreatic function, except that of the Langerhans' cells, is tolerated by both animals and humans is demonstrated by ligation of the pancreatic ducts in dogs, and resection of the head of the pancreas as performed by Whipple[50] in humans. Though both animals and humans survive these procedures, neither digest fats well without the pancreatic enzymes. It is likely that some of the extreme debility seen in ampullary carcinoma is due to interference with the function of the pancreas, but what part of the picture is due to interference with the pancreatic secretions and what part is due to interference with the flow of bile, is speculative. While acute hemorrhagic pancreatitis has never been observed with carcinomata of the ampulla of Vater, Moll and Rouslacroix, *et al.*,[51] have reported acute suppurative pancreatitis, no doubt caused by infection in the ducts. The condition is comparable to suppurative cholangeitis which is seen more commonly.

The gallbladder and common duct are always dilated and are usually thin walled although, if stones are also present, they may be somewhat thickened. The gallbladder usually contains thick, dark bile, but occasionally, as re-

ported by Arnsperger,[44] Kausch[52] and others, it may contain white bile, *i.e.*, thick mucus. Such was the finding in Case 4 of the New York Hospital series. The finding of white bile, then, is not confined to cases of cystic duct obstruction. Invariably the normal flow of green hepatic bile is restored within two to six hours after release of the obstruction.

Clinical Features.—The typical case of carcinoma of the ampulla of Vater has at the onset of symptoms an attack of upper abdominal or epigastric pain followed in a few days by gradually increasing, constant obstructive jaundice, associated with acholic stools, dark urine and pruritus. In the course of time there is rapid loss of weight, and, if the jaundice is long-standing, there may be chills and fever. There may also be a history of biliary colic in the past. On examination the patient usually shows in addition to the deep icterus a smooth enlargement of the liver and a palpable non-tender gallbladder. Roentgenograms commonly show some abnormality in the second portion of the duodenum. A definite anemia is often present and the stools regularly contain occult blood. Untreated, the disease rapidly progresses to a fatal termination. The average duration of life from the first symptom in Outerbridge's series was 7 1/3 months. Mayo-Robson's case lived three years, but ten cases lived less than three months.

Jaundice.—Obstructive jaundice is the outstanding clinical feature of carcinoma of the ampulla of Vater, being present in all of Pallin's 52 cases and 96 per cent of Outerbridge's 110 cases. It was present in 13 out of 14 cases, or 93 per cent, of the New York Hospital series. The jaundice was usually marked, the average icteric index being 121, the lowest 36, the highest 214. In one instance (Case 7) no clinical jaundice was present, and the icteric index was 11. In most cases (85 per cent), the jaundice was of gradual onset and steady; though in two instances (15 per cent) (Cases 3 and 9) it was intermittent. Its average duration in the New York Hospital series was 3.8 months, the shortest eight days, the longest 18 months. It is unusual to have continuous jaundice present for more than 18 months. Rendu[53] suggested that the fluctuations in the jaundice were due to variations in the vascularity of the tumor, and considered intermittency characteristic of ampullary tumors, as contrasted with tumors of the head of the pancreas, in which the jaundice is continuous. Koerte,[54] on the contrary, considered the jaundice in carcinoma of the ampulla of Vater as continuous, in contrast with that present in common duct stones, which is often intermittent. Intermittent jaundice is quite compatible with carcinoma of the ampulla of Vater, especially with the ulcerating tumors which may excavate the ampulla and thereby relieve the obstruction. Durand-Fardel,[55] Carnot,[56] Devic and Savy,[57] Hotz[58] Hartman,[59] Lindner[60] and Morian[61] have reported such cases. Associated with the obstructive jaundice were acholic stools, dark bile stained urine and pruritus.

Pain occurs frequently in carcinoma of the ampulla of Vater, being present in 86 per cent of the New York Hospital series. In 71 per cent it was the first symptom of the disease. Two cases had a past history of biliary colic. The pain usually occurs in the upper abdomen or epigastrium, is cramp-like or

burning in character and usually lasts for only a few days. Occasionally the pain persists and is related to the ingestion of food, in which event duodenal obstruction is likely to be present. Since jaundice usually appears soon after the onset of pain, the pain probably is caused by distention of the gallbladder and bile ducts. There is nothing distinctive about its character in carcinoma of the ampulla of Vater, for similar pain was found by Rienhoff and Lewis[62] in 87 per cent of their cases of carcinoma of the head of the pancreas. The frequent occurrence of pain need not upset the well founded concept of painless jaundice in either of these diseases, for the pain usually disappears before or soon after the onset of jaundice.

Loss of Weight was marked in the New York Hospital series, being present in 78 per cent of cases. The average loss was 19.4, the greatest 40 pounds. It was usually associated with, and at least partially attributable to, anorexia or vomiting.

Anorexia was present as a prominent feature in ten of the 14 cases, or 71 per cent. In the other four cases the appetite remained good in spite of practically complete obstructive jaundice.

Vomiting is not a prominent symptom of ampullary tumors, occurring in but 36 per cent of the New York Hospital series. In three cases it was associated with the pain, and in the other two there was vomiting without pain. When vomiting persists over a period of time, duodenal obstruction is usually found. The emesis is notably free of bile.

Diarrhea has been mentioned as a common symptom of ampullary tumors, particularly by Denechau, *et al.*,[63] who noted marked diarrhea in eight out of 23 or 35 per cent of cases. They emphasized that obstructive jaundice, intestinal bleeding and diarrhea are the diagnostic features of importance in ampullary tumors. In their series these were certainly fairly constant findings, and for this reason, diarrhea should carefully be considered in the diagnosis of each individual case. In the New York Hospital series, however, diarrhea was a prominent feature in but three instances, or 21 per cent of cases.

Palpable Gallbladder.—In all cases of carcinoma of the ampulla of Vater the gallbladder is distended with bile, and if the organ has not previously been fibrosed by infection and is not obscured by the edge of the liver, it is enlarged to such a degree that it becomes clinically palpable. In extreme conditions the gallbladder may be so enormous that it may be felt by pelvic examination, or, as in Case 8, medial to the right iliac spine. Rarely, as in the cases of Coats and Finlayson[64] and May,[65] does the gallbladder perforate. Since the palpability of any mass depends largely upon the astuteness of the observer, there is considerable variation in the frequency with which the organ is felt. It is often felt by the surgeon, but not recorded by the house officer, which emphasizes the value of experience in palpating this elusive viscus. Palpation under anesthesia before making the incision is often helpful. In the New York Hospital series, the gallbladder was felt in 50 per cent of cases, but in all except Case 7, operation or postmortem examination

showed an organ sufficiently enlarged to have been palpable. It is usually not tender, though in two cases of this series moderate tenderness was elicited.

Enlargement of the Liver is always present and was detected clinically in all but two cases, *i.e.*, in 86 per cent of the New York Hospital series. The enlargement is usually moderate, its lower border seldom progressing beyond the level of the umbilicus. The edge of the liver is usually smooth, firm and nontender, but if cholangeitis is present, pressure may cause pain.

Chills and Fever are not uncommon in patients with obstructive jaundice, but are probably less common in obstruction due to tumor than in that due to stones. The chills and fever are presumptive evidence of cholangeitis; and if the liver is tender, possibly of hepatic abscesses. The elevation of temperature is of the intermittent Charcot type and may be alarmingly persistent. Five cases, or 36 per cent of the New York Hospital series had intermittent fever. In two instances (Cases 4 and 9) there were chills and both of these had miliary abscesses in the liver.

Ascites was noted but three times in Outerbridge's 110 cases. In the New York Hospital series, Case 7 had clinical evidence of abdominal fluid before death, and also had bilateral bloody pleural effusion due to pleural metastases. These are rare findings, however, and are not an integral part of the clinical picture of carcinoma of the ampulla of Vater.

Gastro-Intestinal Bleeding.—In the literature on ampullary carcinoma, gastro-intestinal bleeding and the presence of occult blood in the stools has received but little attention, most of the comment having been reserved for the occasional case that had gross melena. Outerbridge found intestinal hemorrhage mentioned but twice in his 110 collected cases. Ewing describes a papillary tumor, 5 Mm. in diameter, which caused a fatal hemorrhage. Cases 3 and 5 of the New York Hospital series died of hemorrhage from the tumor. In Case 5 the superior mesenteric artery was eroded. Though mentioned by most authors, occult blood in the stools was not emphasized until Denechau, *et al.*, in 1931, found evidence of bleeding in the stools of many of their cases. At the New York Hospital, repeated examinations for occult blood in the stools have been made on patients with obstructive jaundice, and on the basis of this test, ulcerating or oozing lesions of the gastro-intestinal tract have been suspected. In 11 out of the 14 cases in this series, the stools were examined and in nine, or 82 per cent, there was persistent, strongly positive evidence of occult blood in the stools. The cases in which no evidence of bleeding was found were Case 1, which had but one stool tested, and Case 7, in which the tumor did not erode the duodenal mucosa.

From this evidence it is felt that repeated examinations of the stools for occult blood are most important in the diagnosis of ampullary carcinoma; indeed, this is the one distinctive feature about the disease; the only one not regularly encountered in obstructive jaundice due to other causes. As a criterion it is not without its pitfalls, however, for all cases of long-standing jaundice may have cholemic hemorrhages. Rienhoff and Lewis found occult blood in the stools in 21 per cent of their pancreatic carcinomata; and this

finding was misleading in a case of carcinoma of the common duct seen at the New York Hospital. In general, the gastro-intestinal bleeding in obstructive jaundice from other causes is intermittent, while in ampullary carcinoma it is persistent, giving positive tests in all stools. For this reason it is important to test every stool over a period of time before operation. The surgical procedure often initiates cholemic hemorrhages in jaundiced cases, postoperative hemorrhage accounting for about 50 per cent of the immediate mortality after operation. Accordingly, tests of stools during the first two weeks after operation are of little or no value.

Anemia is occasionally a striking feature of carcinoma of the ampulla of Vater. It is of the secondary type, and most marked in cases that have bleeding from the tumor, *i.e.*, in cases with ulcerating tumors. In the New York Hospital series the average hemoglobin was 71 per cent; the average erythrocyte count 3,700,000. In five instances (Cases 2, 3, 4, 5 and 9), or 36 per cent, anemia was a prominent clinical feature when the patient entered the hospital. In Case 4, the anemia was so marked that the patient had peripheral edema.

Duodenal Drainage.—The duodenal tube may be a very helpful diagnostic aid. Crohn,[66] and more recently Chiray, *et al.*,[67] have emphasized the importance of duodenal drainage in the diagnosis of ampullary carcinoma. In the New York Hospital series duodenal drainage was done on four of the 14 cases. In Cases 1 and 12 the return was clear mucus, but in Cases 4 and 5 fresh blood was obtained. In no cases did any bile return through the tube. The aspiration of fresh blood from the duodenum supports the evidence of occult blood in the stools.

Roentgenographic Examination.—Though the literature is singularly free of references to the roentgenographic diagnosis of carcinoma of the ampulla of Vater, roentgenographs have been particularly helpful in the New York Hospital series. Ten of the 14 cases had gastro-intestinal series, and 80 per cent of these showed some abnormality in the second portion of the duodenum. A summary of the findings follows:

(1) Obstruction at the level of the ampulla, with dilatation of the first portion of the duodenum and stomach was found in 50 per cent of the cases (Cases 1, 2, 3, 9 and 11).

(2) Definite sharply outlined filling defects at the ampulla in 10 per cent (Case 7).

(3) Flattening of the duodenum from behind, in 10 per cent (Case 5).

(4) Irritability of the second portion of the duodenum in 10 per cent (Case 14).

(5) Normal gastro-intestinal series in 20 per cent (Cases 8 and 12).

These findings received various interpretations by the roentgenologists, but the important feature to the clinician is to know there is some lesion in the second portion of the duodenum. A lesion having been discovered, it then becomes the problem to determine whether it is caused by carcinoma of the ampulla of Vater or carcinoma of the head of the pancreas. The

roentgenographic differential diagnosis is virtually limited to these two conditions, for carcinoma of the common duct usually causes no duodenal defect. Carcinoma of the head of the pancreas may cause widening of the duodenal loop, or anterior displacement of the duodenum, but rarely does it cause the duodenal obstruction or filling defect seen in ampullary tumors.

DIAGNOSIS.—Throughout the literature the difficulty in the differential diagnosis of carcinoma of the ampulla of Vater has been emphasized. Most authors express the opinion that there is little hope of a correct diagnosis without exploration. The experience in the New York Hospital series fails to support this view. It is the author's opinion that careful clinical and laboratory study of a series of cases of obstructive jaundice brings out subtle differences which are highly important to correct diagnosis.

The greatest contribution to differential diagnosis of obstructive jaundice probably is that of Courvoisier,[68] whose observations were sufficiently fundamental to take the form of a law. Simply stated, Courvoisier's law is as follows: In obstructive jaundice if the gallbladder is enlarged, the obstruction is due to tumor; if not enlarged the obstruction is due to stones. Exceptions to Courvoisier's law are few and these rarely cause confusion. Notable exceptions are: (1) Hydrops of the gallbladder due to a stone which not only obstructs the cystic duct, but also impinges on the common duct and causes jaundice. The clinical picture of hydrops of the gallbladder is quite distinctive and unlikely to be confused with that of tumor obstructing the common duct. (2) Carcinoma of the common hepatic duct causes obstructive jaundice without enlargement of the gallbladder, and is extremely difficult to differentiate from jaundice due to "silent" stones. The condition is rare, however, and because the gallbladder is not palpable, is unlikely to be confused with carcinoma of the ampulla of Vater. (3) The gallbladder is not always enlarged in tumors obstructing the common duct. The organ may be so thickened and fibrotic from long-standing cholecystitis and cholelithiasis that it is no longer distensible by the hydrostatic pressure of the bile. It is in this condition that Courvoisier's law most frequently fails.

The criterion of the presence of a palpable gallbladder divides obstructive jaundice into two groups with considerable accuracy. The chief concern in carcinoma of the ampulla of Vater is to differentiate it from other tumors which cause a palpable gallbladder. The most common of these are (1) carcinoma of the head of the pancreas and (2) carcinoma of the common duct. All of these tumors cause very similar clinical pictures, but it is our experience that persistent occult blood in the stools, anemia and roentgenographic changes in the second portion of the duodenum serve to differentiate carcinoma of the ampulla of Vater in a high percentage of cases. It is felt, therefore, that the diagnosis of ampullary carcinoma is possible, and that it can often be made with reasonable certainty.

TREATMENT AND RESULTS.—The sole purpose of the diagnosis of carcinoma of the ampulla of Vater should be to hasten its surgical treatment. Ampullary carcinoma, more than any of the numerous malignant lesions of

the gastro-intestinal and biliary tracts, gives dramatic early symptoms which facilitate diagnosis while the tumor remains localized. For this reason a high percentage of these tumors are operable when first seen by the surgeon. But the very same factors which make early diagnosis possible, make surgical treatment difficult and therein lies the explanation of the generally poor operative results. The long-standing obstructive jaundice and poor physical condition unite with the technical difficulties to create a situation that is often insurmountable. Yet with time and experience, the technical difficulties will be overcome and more operative cures of carcinoma of the ampulla of Vater should be obtained.

The literature on ampullary carcinoma has been concerned chiefly with the operative treatment and results, the cases having been repeatedly collected and summarized. Because of the rarity of the disease, no one surgeon has had wide experience in its treatment, and collected cases must form the basis of study.

The operative treatment may be divided into (1) palliative operations and (2) radical resections.

(1) *Palliative Operations.*—(a) Cholecystostomy.—In the presence of long-standing jaundice and extreme debility, or suppurative cholangeitis, radical procedures usually cannot be effected. Cholecystostomy, while not the procedure of choice, is indicated in cases which will not tolerate cholecystogastrostomy or resection and should be carried out under local anesthesia through a small incision without abdominal exploration. Though the operator is unable to determine the extent of the pathologic lesion in this procedure, he does not subject his patient to the added risk of exploration; this should be delayed until a time when the case will at least tolerate a cholecystogastrostomy.

The ultimate benefits of a cholecystostomy to the patient are open to question. The immediate benefits, however, are often striking. In the New York Hospital series, cholecystostomy was performed five times (Cases 2, 4, 8, 9 and 12). The abdomen was explored at the same time in all cases and in Case 8 duodenostomy and biopsy of the tumor were performed. Cases 2 and 12 were operative deaths, an operative mortality of 40 per cent. Case 2 died on the twenty-ninth postoperative day of gastro-intestinal hemorrhage while Case 12 died on the fifth postoperative day of bleeding from the wound and bronchopneumonia. Cases 4, 8 and 9 survived for an average of six months after cholecystostomy and their lives were made much more comfortable by this procedure.

(b) Cholecystogastrostomy.—The ideal palliative operation for any type of common duct obstruction is cholecystogastrostomy, as it releases the obstruction without the loss of bile. Cholecystogastrostomy takes preference over cholecystoduodenostomy particularly in ampullary carcinoma, for it paves the way for radical resection and places the anastomosis where it is unlikely to become secondarily infiltrated and obstructed by tumor. Unfortunately, cholecystogastrostomy in ampullary carcinoma has a high operative mortality,

the figure approaching 70 per cent according to Muller and Rodemaker.[69] The reason for the high mortality is to be found in the tendency to bleed and the poor condition of the patient; therefore, it must be emphasized that cholecystogastrostomy can be performed after cholecystostomy, and should be delayed until, in the judgment of the operator, the patient has a good chance of surviving the procedure.

Anastomoses for the relief of biliary obstruction were performed in seven cases of the New York Hospital series with three operative deaths, an operative mortality of 43 per cent. In five cases, cholecystogastrostomy was performed with two operative deaths. Case 4 had had a previous cholecystostomy and died of peritonitis on the third day after cholecystogastrostomy. In Case 11, both duodenostomy and cholecystogastrostomy were performed, and the patient died of peritonitis on the fifteenth postoperative day. Choledochoduodenostomy was performed in Case 6 and the patient died of peritonitis on the third postoperative day. Cholecystoduodenostomy was performed in Case 13 with a highly satisfactory immediate result, though we do not know how long the patient survived after operation. In Cases 9, 10 and 14, cholecystogastrostomy was highly successful, the patients surviving for an average of 11 months after operation. Case 10 lived *22* months and worked until six months before death.

In spite of the high mortality, it is felt that cholecystostomy or cholecystogastrostomy offer the survivor such symptomatic relief that patients should be subjected to them. But these procedures should be planned as a preliminary step in preparing the patient for radical removal of the tumor if and when his condition warrants.

(2) *Radical Operations.*—In 1935, Hunt and Budd published all the available data on radical operations for the treatment of ampullary carcinoma. Transduodenal resection is well illustrated and described in their article. Their analysis of 76 cases is shown in Table I.

TABLE I

ANALYSIS OF 76 CASES OF RADICAL REMOVAL OF AMPULLARY CARCINOMA

(*Hunt and Budd*[8])

Operation	Cases	Deaths	Per Cent
Transduodenal Excision	63	24	38
Transduodenal excision only	20	9	45
Transduodenal excision with reimplantation of ducts	19	4	21
Transduodenal excision with reimplantation of ducts with internal or external drainage	11	5	45.4
Transduodenal excision without reimplantation of ducts, with internal or external drainage	13	6	46
Resection of Duodenum	9	3	33
Retroduodenal Excision	4	2	50
Total to 1934	76	29	39.77
Survivals	47		61.9

It would seem apparent, therefore, from the statistics of Hunt and Budd (Table I) that transduodenal resection with reimplantation of the ducts offers the patient more than any other procedure from the viewpoint of operative mortality. It is impossible, however, to classify the various procedures from the point of view of end-results, for many of the cases were reported too soon after operation. There are, however, a certain amount of data available. Recurrences have been frequent following radical operation for ampullary carcinoma. Ten of the 47 cases that survived operation lived less than one year, and numerous cases required further operative relief for recurring jaundice or duodenal obstruction.

Muller and Rodemaker cite seven cases living four years or longer after operation (Table II). It is interesting that transduodenal resection with reimplantation of the ducts was performed upon all of these patients.

TABLE II

CASES SURVIVING TRANSDUODENAL RESECTION OF AMPULLARY CARCINOMA AFTER FOUR YEARS

(*Muller and Rodemaker*[69])

AUTHOR	LIVING	STATUS
Koerte[70]	22 yrs.	Symptom free
Lewis[71]	9 yrs.	Symptom free
Oehler[46]	6 yrs.	Symptom free
VanRemynse[72]	6 yrs.	Not known
VanArdenne[72]	5 yrs.	Not known
Clar[73]	5 yrs.	Died
Oliani[74]	4 yrs.	Symptom free

Hunt and Budd add an eighth case, that of Cabot reported by Potter,[75] living and well eight years after transduodenal resection with reimplantation of the ducts. Since Clar's[73] case died, there are probably seven cures out of 76 cases, or about 9 per cent. Whereas this is a rather poor showing for radical surgery, it is strongly felt that cures will be more common in the future through the prudent use of palliative procedures to improve the condition of the patients.

In view of the pathology of carcinoma of the ampulla of Vater, it is obvious that no single radical operation is suited to all variations of the disease. If the tumor is small, papillary, free of ulceration and more or less pedunculated without infiltration at its base, transduodenal resection with reimplantation of the ducts should be the ultimate procedure. If the tumor is ulcerating and infiltrates the duodenal wall, transduodenal resection obviously is not the procedure of choice from the viewpoint of permanent cure. To this end Whipple, *et al.*, have made a very practical contribution to the surgical treatment of ampullary carcinoma in their newly devised operation. The procedure is carried out in two stages as follows:

First Stage: (1) Posterior gastro-enterostomy.

(2) Ligation and section of the common duct below the cystic duct after

determining the patency of the cystic duct, and leaving a long, slack silk ligature as an indicator on the lower stump of the sectioned common duct.

(3) Cholecystogastrostomy to the anterior surface of the stomach well away from the pylorus, using an anastomotic opening at least 2 cm. in diameter.

Three or four weeks later, the second stage is undertaken.

Second Stage: (1) Ligation of the pancreaticoduodenal and gastroduodenal arteries.

(2) Resection of the descending portion of the duodenum with inversion of the upper and lower ends, and a V-shaped excision of the head of the pancreas and common duct, using the silk ligature on the duct as a guide to the end of the duct.

(3) Ligation of the cut end of the duct of Wirsung and duct of Santorini, if present, and suturing of the two cut surfaces of the pancreas with interrupted sutures of fine silk.

(4) Drainage of the bed of the resected duodenum with a cigarette drain.

Nothing short of this type of radical and wide resection would appear to offer a cure for the more malignant ampullary carcinomata. It is conceivable that preliminary cholecystostomy would place the patient in condition to tolerate the extensive procedure. The entire resection as outlined by Whipple, could, if necessary, be carried out in the presence of a cholecystostomy.

CONCLUSIONS

It is believed that the surgical treatment of carcinoma of the ampulla of Vater may be compared to that of carcinoma of the bowel. The first procedure should be directed toward the relief of the biliary obstruction and the second toward the removal of its cause either by transduodenal resection or by radical resection of the duodenum and head of the pancreas. If it is possible to make a diagnosis, these surgical procedures can be planned ahead and the problem attacked with a degree of surety of purpose.

CASE HISTORIES

Case 1.—*History.*—A white male, age 49, was in good health until seven months before admission, when he had cramp-like epigastric pains lasting two days followed immediately by painless, progressively increasing jaundice, clay-colored stools, dark urine and pruritus. For two weeks before admission the patient vomited every night and lost five pounds in weight.

Physical Examination.—A deeply jaundiced but well nourished male. Temperature and pulse normal. Heart and lungs essentially normal. The upper abdomen appeared distended but was soft. The edge of the liver was smooth, slightly tender and descended 3 cm. below the right costal margin. The abdomen was not tender and no masses were felt. The gallbladder was not palpable.

Roentgenographic Examination.—The gastro-intestinal series showed a tremendously dilated stomach with obstruction of the second portion of the duodenum.

Laboratory Data.—The urine was deeply bile stained; red blood cells, 4,800,000; hemoglobin, 85 per cent; white blood cells, 10,400; icteric index, 150. The only

stool tested was acholic and negative for occult blood. Duodenal drainage returned clear mucus without bile.

Course.—The patient gradually went downhill and died nine days after admission, seven and one-half months after the first symptom.

Postmortem.—The stomach and first portion of the duodenum were greatly dilated. There was an annular constriction of the second portion of the duodenum completely closing the lumen at the level of the ampulla of Vater and caused by infiltration of a tumor mass about 4 cm. in diameter. The tumor centered about the ampulla of Vater, constricting the lumen of both the common duct and pancreatic ducts and infiltrated the head of the pancreas slightly. The ampullary region appeared granular and pinkish white. There were no metastases to the regional nodes or liver. The gallbladder was greatly dilated and thin walled, as were the biliary and pancreatic ducts. There were no biliary calculi.

Microscopic Examination.—Columnar cell adenocarcinoma.

Case 2.—*History.*—A Swedish woman, age 47, for 18 months before admission had occasional attacks of epigastric pain associated with tenderness over the gallbladder. Five weeks before admission she began having constant burning epigastric pain unrelated to food, vomiting of practically all food ingested and alternate constipation and diarrhea. Jaundice, clay colored stools and dark urine developed two weeks before admission. She had fever on several occasions and lost 35 pounds in weight in five weeks.

Physical Examination.—A poorly nourished, moderately jaundiced woman with a slight elevation of temperature. There was moderate epigastric tenderness. The edge of the liver was smooth and 3 cm. below the right costal margin. The gallbladder was not palpable.

Roentgenographic Examination.—This revealed that the stomach and the first portion of the duodenum were moderately dilated. The second portion of the duodenum was constricted. The gallbladder failed to visualize by Graham test.

Laboratory Data.—The urine was bile stained. Red blood cells, 3,600,000; hemoglobin, 56 per cent; white blood cells, 3,900; icteric index, 46. All stool specimens were strongly positive for occult blood.

Operation.—Cholecystostomy. The gallbladder was moderately distended, thin walled and free of stones. The common duct was twice the normal size. There was a nodular mass, 4 cm. in diameter, in the second portion of the duodenum.

Course.—The patient had gastro-intestinal hemorrhages following operation, she gradually went downhill and died of hemorrhage on the twenty-ninth postoperative day.

Postmortem.—The liver was studded with metastatic nodules reaching 4 cm. in diameter. The gallbladder was small, thick walled and free of stones. The biliary and pancreatic ducts were all dilated and the pancreas was fibrotic. At the ampulla of Vater there was an ulcerating, infiltrating, friable tumor 3 cm. in diameter which excavated the ampulla and partially obstructed both the pancreatic and common bile ducts. There were metastases to the periportal, pancreatic and retroperitoneal nodes.

Microscopic Examination.—Adenocarcinoma with moderate desmoplastic reaction.

Case 3.—*History.*—An Armenian woman, age 40, was well until 16 months before admission when she developed painless obstructive jaundice. Operation at another institution revealed a common duct stone which was removed, but the gallbladder was not resected. Subsequently the patient was well until two months ago when she began to have steady dull epigastric pain. Two weeks later she vomited all food for one week. In two months she lost 20 pounds, but has noted no jaundice.

Physical Examination.—A rather poorly nourished woman with a definite icteric tint to the skin. The temperature and pulse were normal. There was moderate tenderness in the epigastrium. The liver and gallbladder were not felt.

Roentgenographic Examination.—The gallbladder visualized faintly after the dye. The common duct and hepatic duct and part of the gallbladder were filled with air, suggesting fistula formation. A gastro-intestinal series showed the stomach and first

part of the duodenum to be dilated with a constriction in the second portion of the duodenum.

Laboratory Data.—The urine was slightly blood-tinged. Red blood cells, 3,000,000; hemoglobin, 46 per cent; white blood cells, 14,300; icteric index, 36. All stool specimens were strongly positive for occult blood.

Course.—The patient ran a low grade fever and died suddenly of gastro-intestinal hemorrhage four weeks after admission, 17 months after her first jaundice.

Postmortem.—The region of the ampulla of Vater formed the center of a mass roughly 6 cm. in diameter which infiltrated and obstructed the duodenum at that level, and extended upwards into the lumen of the first portion of the duodenum. The mass infiltrated the head of the pancreas, the portal vein and a loop of adherent jejunum. The tumor was soft, friable and necrotic. The periportal and peripancreatic nodes were all involved. The liver was studded with metastatic nodules up to 1 cm. in diameter. The common and pancreatic ducts entered the duodenum together at the base of an ulcerated crater and were both stenosed at this point. Proximally the biliary and pancreatic ducts were greatly dilated. There was a fistulous tract between the dilated common duct and the first portion of the duodenum, which admitted a probe.

Microscopic Examination.—Adenocarcinoma, much of which is necrotic and infected.

Case 4.—*History.*—An Italian male, age 38, was well until 18 months before admission when he had an attack of upper abdominal pain lasting a few days followed by the gradual onset of progressively deepening jaundice, dark urine, pruritus and clay colored stools. In the past four months he noted edema of the legs, and the last month had intermittent chills and fever. In spite of a good appetite he had lost 18 pounds in weight.

Physical Examination.—A fairly well nourished Italian male with deep greenish jaundice. The temperature ranged from 39° to 40° C. every night with occasional chills. The liver was felt 8 cm. below the right costal margin and was moderately tender. The gallbladder was not felt. There was moderate pitting edema of the ankles.

Laboratory Data.—The urine was deeply bile stained. Red blood cells, 2,200,000; hemoglobin, 32 per cent; white blood cells, 8,800; icteric index, 93. All stools were strongly positive for occult blood. Duodenal drainage produced fresh blood.

First Operation.—Cholecystostomy. The liver was found studded with grayish, softened areas. The gallbladder was greatly distended with white bile but was free of stones. The common duct was twice the normal size. The head of the pancreas was indurated but no tumor was felt.

Course.—The biliary fistula drained between 1,000 and 1,500 cc. of bile daily, which was administered to the patient by stomach tube. The temperature subsided, the jaundice disappeared and the patient was well for three months, except for the biliary fistula. He then developed a profound anemia, weakness and edema of the legs, for which he was readmitted four months after the first admission.

Second Operation.—Cholecystogastrostomy. The patient died on the third postoperative day.

Postmortem.—The immediate cause of death was peritonitis. The biliary and pancreatic ducts were all dilated and entered the duodenum 1.5 cm. apart. The openings of both ducts were surrounded and partially obstructed by a slightly elevated, soft necrotic tumor, 3 cm. in diameter, which did not obstruct the duodenum or infiltrate the head of the pancreas. There were no metastases to the regional nodes. There were several metastatic nodules, 1 cm. in diameter, in the liver.

Microscopic Examination.—Columnar cell adenocarcinoma.

Case 5.—*History.*—An Irish male, age 44, in good health until two and one-half months before admission, when he had a feeling of epigastric discomfort lasting two days, followed shortly by a steady, gradually increasing jaundice and gnawing epigastric pain after meals. With this pain he had loose, watery stools for three weeks associated

with poor appetite and loss of 35 pounds in weight. On the day of admission he had a sudden attack of faintness, dizziness, diaphoresis and dyspnea.

Physical Examination.—A fairly well nourished, pale, deeply jaundiced patient with normal temperature. The edge of the liver was smooth and 6 cm. below the costal margin. The gallbladder was felt, descending below the edge of the liver.

Roentgenographic Examination.—The gastro-intestinal series showed nothing abnormal save for a slight flattening of the duodenum from behind.

Laboratory Data.—The urine was deeply bile stained. Red blood cells 2,600,000; hemoglobin, 60 per cent; white blood cells, 11,600; Wassermann, four plus positive; icteric index, 160. All stool specimens were strongly positive for occult blood. The duodenal drainage contained mucus followed by blood; no bile was obtained.

Course.—The patient had repeated gastro-intestinal hemorrhages and died of these one and one-half months after admission, four months after onset of the illness.

Postmortem.—The gastro-intestinal tract was filled with blood. The liver was studded throughout with tumor nodules as large as 1 cm. in diameter. The gallbladder and biliary ducts were dilated but free of stones. At the ampulla of Vater there was an ulcerated tumor, 2 cm. in diameter, with a crater-like base through which the common and pancreatic ducts entered separately. The opening of both ducts was practically closed off by the tumor which infiltrated the head of the pancreas slightly. The regional nodes were full of metastases. A large artery at the base of the carcinomatous crater had eroded.

Microscopic Examination.—Adenocarcinoma.

Case 6.—*History.*—A white female, age 56, had intermittent biliary colic for one year, six years ago and was then well until three weeks before admission when she began to have chills and fever associated with steady, painless jaundice and diarrhea. She lost 12 pounds in three weeks.

Physical Examination.—A well nourished, deeply jaundiced woman with a mild intermittent fever. The liver was felt 8 cm. below the right costal margin and the gallbladder was palpable below that point.

Roentgenographic Examination.—A flat film of the abdomen showed questionable gallstones.

Laboratory Data.—The urine was bile stained. Red blood cells, 4,500,000; hemoglobin, 85 per cent; white blood cells, 12,450; icteric index not recorded. All stools were strongly positive for occult blood.

Operation.—Cholecystectomy and choledochoduodenostomy. The gallbladder was greatly dilated and contained several small stones. The common duct was 3.5 cm. in diameter. No mass was felt at the ampulla of Vater.

Course.—The patient died on the third postoperative day with signs of peritonitis and pneumonia, one month after the onset of symptoms.

Postmortem.—There was a leak in the anastomosis and a generalized bile peritonitis. The pancreatic and biliary ducts were dilated and entered the duodenum together. Their openings were occluded by a papillary, fungating, mass 2 cm. in diameter, which had its origin in the upper half of the ampulla of Vater and projected into the duodenum. No metastases were present.

Microscopic Examination.—Adenocarcinoma.

Case 7.—*History.*—A white male, age 59, was in good health till three months before admission when he began to lose weight. There was no definite symptomatology until one month before admission when he noted weakness, anorexia and daily cramp-like para-umbilical pains. He lost 20 pounds in three months.

Physical Examination.—A pale, undernourished man with normal temperature and no jaundice. There were hard, shotty, bilateral supraclavicular nodes and signs of fluid at the base of the right lung. The edge of the liver was smooth and firm about 8 cm. below the right costal margin. There was an indefinite deep mass felt about and above the umbilicus.

Roentgenographic Examination.—A gastro-intestinal series showed a defect on the posterior wall of the second portion of the duodenum with suggestive displacement of the duodenal loop to the right.

Laboratory Data.—The urine contained pus. The two stools examined contained no occult blood. Red blood cells, 3,900,000; hemoglobin, 80 per cent; white blood cells, 12,000; icteric index, 11.

Biopsy.—A supraclavicular node, 1 cm. in diameter, was composed of solid metastatic alveolar carcinoma.

Course.—The patient developed bilateral hydrothorax requiring repeated tapping. The fluid was always grossly bloody. He went downhill rapidly and died one month after admission and four months after the onset of symptoms.

Postmortem.—Originating in the submucosa in the region of the ampulla of Vater and infiltrating the duodenal wall and head of the pancreas was a mass, 3 cm. in diameter. The mucosa was intact and there was no ulceration. The mass constricted the common duct at the ampulla of Vater so that it would just admit a 1.5 cm. probe. There were several nodules 3 Mm. in diameter on the serosal surface of the liver but no metastases in the substance of the liver. The visceral and parietal peritoneum and omentum were studded with small metastatic nodules. The epigastric mass was composed of a mass of retroperitoneal and mesenteric nodes. These nodes extended down into the lumbar region and the perirectal fat was densely infiltrated by tumor tissue. The rectal mucosa was intact. There were numerous metastatic nodules in the visceral and parietal pleurae, most of them being in the right lower thorax. There were several small metastatic nodules in the right lower lobe and the supraclavicular nodes were bilaterally involved.

Microscopic Examination.—The primary tumor seemed to arise in the submucosa of the peri-ampullary duodenum in the region of Brunner's glands, replacing these glands with cords of malignant cells which infiltrated normal pancreas and duodenal wall and constricting the ampulla of Vater incidentally. The tendency to alveolar formation was very slight.

Case 8.—*History.*—An Irish male, age 43, was in good health until five months before admission when he had an attack of acute epigastric pain followed in the course of 24 hours by gradually increasing, steady jaundice, pruritus, clay colored stools and anorexia. He lost 40 pounds in weight.

Physical Examination.—A poorly nourished, deeply jaundiced white man with a normal temperature. The edge of the liver was smooth and at the level of the umbilicus. The gallbladder was palpable below the edge of the liver.

Roentgenographic Examination.—The gastro-intestinal series was normal.

Laboratory Data.—The urine was deeply bile stained. Icteric index, 80. No stools were examined for occult blood.

Operation.—Cholecystostomy, duodenostomy and biopsy. The gallbladder measured 6x20 cm. and was free of stones. The common duct was 2.5 cm. in diameter. A mass could be felt in the duodenum at the ampulla. The duodenum was opened and a biopsy taken of friable, papillary and ulcerating tissue forming a mass 2 cm. in diameter and situated at the ampulla of Vater.

Course.—The jaundice cleared and the patient was discharged with a biliary fistula. He died six months after admission and 11 months after the onset of the illness. No autopsy was performed.

Microscopic Examination.—The biopsy showed solid sheets of cancer cells, with no tendency to alveolar formation.

Case 9.—*History.*—An Italian male, age 42, eight months before admission began to have upper abdominal pain and occasional vomiting, which was followed shortly by deep painless jaundice lasting two months. He was then well for two months, but four months before admission the jaundice returned and remained constant, associated with clay colored stools and marked pruritus. He lost 14 pounds and had chills and fever for one month.

Physial Examination.—The patient was thin, pale and deeply jaundiced. His temperature rose to 40° C. every night and was usually preceded by a chill. The edge of the liver was slightly tender and 2 cm. below the right costal margin. The gallbladder was palpable on the liver margin.

Roentgenographic Examination.—A gastro-intestinal series showed the stomach and first portion of the duodenum to be dilated with a constriction in the second portion of the duodenum. The gallbladder failed to visualize after the dye.

Laboratory Data.—The urine was deeply bile stained. Red blood cells, 2,400,000; hemoglobin, 45 per cent; white blood cells, 18,000; icteric index, 100. All stools were strongly positive for occult blood.

First Operation.—Cholecystostomy. The liver was studded with miliary abscesses. The gallbladder was greatly dilated but free of stones.

Course.—The patient drained 1,000 to 1,500 cc. of bile daily which was administered to him by stomach tube. The jaundice cleared and the patient gained back all the lost weight. The stools always contained occult blood. He was readmitted three months after the first admission.

Second Operation.—Cholecystogastrostomy. An irregular, stony hard mass 3 cm. in diameter was felt in the ampulla of Vater. There was no evidence of metastases and the head of the pancreas was not infiltrated.

Course.—The patient remained well for two months, then developed chills and fever and a biliary fistula in the old wound. He died five months after the second operation, 17 months after the onset of symptoms. No postmortem was obtained.

Case 10.—*History.*—An Italian male, age 50, was in good health until six weeks before admission when he suffered the gradual onset of steady jaundice associated with clay colored stools and pruritus. His appetite was good and he lost no weight.

Physical Examination.—A deeply jaundiced but well nourished male with a normal temperature. The edge of the liver was felt just below the costal margin and on its border there was a questionably palpable gallbladder.

Roentgenographic Examination.—The gallbladder failed to visualize, after dye.

Laboratory Data.—The urine was deeply bile stained. Red blood cells, 5,000,000; hemoglobin, 100 per cent; white blood cells, 6,500; icteric index, 214. All stools were strongly positive for occult blood.

Operation.—Cholecystogastrostomy. The gallbladder and common duct were greatly dilated but free of stones. There was a hard mass 2 cm. in diameter in the duodenal wall at the ampulla of Vater. There were no metastases.

Course.—The patient recovered from operation and the jaundice cleared. He remained quite well for 11 months, when he began to have epigastric pain, loss of weight and enlargement of the liver. He gradually went downhill and died 22 months after operation and 24 months after the onset of symptoms. Postmortem examination was not made.

Case 11.—*History.*—A Hebrew woman, age 50, was in good health until six weeks before admission when she had epigastric cramp-like pain associated with daily vomiting which lasted three weeks. One month ago she noted jaundice which gradually increased and was associated with pruritus and clay colored stools. She lost some weight.

Physical Examination.—A deeply jaundiced, poorly nourished woman with a normal temperature. The edge of the liver was smooth and firm and 2 cm. below the right costal margin. The gallbladder was not felt.

Roentgenographic Examination.—The gallbladder was not visualized by dye. A gastro-intestinal series showed slight dilatation in the first portion of the duodenum and stasis in the second portion.

Laboratory Data.—The urine was deeply bile stained. Red blood cells, 3,900,000; hemoglobin, 84 per cent; white blood cells, 8,900; icteric index, 100. All stools were strongly positive for occult blood.

First Operation.—Cholecystogastrostomy and duodenostomy. The gallbladder was

large, distended but free of stones. The common duct was 3.5 cm. in diameter. There was a hard, nodular, movable mass 4x3 cm. in the second portion of the duodenum which did not involve the pancreas. There were no metastases. On opening the duodenum, a tumor 3 cm. in diameter with a central ulcerating crater was found at the ampulla.

Course.—After a stormy course complicated by signs of pneumonia and peritonitis, the patient died on the fifteenth postoperative day, nine weeks after the onset of symptoms. No postmortem was obtained.

Case 12.—*History.*—An Italian male, age 55, was well until five weeks before admission when he began to have vague epigastric discomfort, followed shortly by painless, progressive jaundice and associated with pruritus and clay colored stools.

Physical Examination.—A deeply jaundiced but well nourished male with a normal temperature. The edge of the liver was smooth and not tender and felt 6 cm. below the right costal margin. On its edge a large, moderately tender gallbladder could be palpated.

Roentgenographic Examination.—A gastro-intestinal series was negative.

Laboratory Data.—The urine was deeply bile stained. Red blood cells, 4,000,000; hemoglobin, 80 per cent; white blood cells, 7,900; icteric index, 150. Duodenal drainage returned clear mucus with no bile. The stools were not tested for occult blood.

Second Operation.—Cholecystostomy. The gallbladder was distended and free of stones. The common duct was twice the normal size. At the ampulla of Vater a hard mass, 2 cm. in diameter, could be felt in the duodenal wall. The pancreas was free and there were no metastases.

Course.—The postoperative course was complicated by bleeding from the wound. The patient died on the fifth postoperative day of bronchopneumonia. No postmortem was obtained.

Case 13.—*History.*—A Hebrew woman, age 46, had attacks of rather typical biliary colic for 11 years before admission. Some of these attacks were followed by jaundice. Cholecystostomy with removal of stones was performed two years before this admission, but there was no relief from the attacks of pain. For two months before admission, she had deep continuous jaundice with occasional slight pain in the right upper quadrant.

Physical Examination.—A well nourished, deeply jaundiced woman with a low grade fever. There was marked tenderness in the right upper portion of the old scar but no masses could be felt.

Laboratory Data.—The urine was deeply bile stained. White blood cells, 7,000. The stools were not tested for occult blood.

Third Operation.—Cholecystoduodenostomy and duodenotomy. The gallbladder and common duct were greatly distended. A mass was palpable in the duodenum. On opening the duodenum a hard, ulcerating tumor, 4 cm. in diameter, was found at the ampulla of Vater. This was biopsied. The pancreas was normal and there were no metastases.

Course.—The jaundice cleared after operation and the patient was discharged in good condition. She was not followed.

Microscopic Examination.—Infiltrating adenocarcinoma with moderate desmoplastic reaction.

Case 14.—*History.*—A white male, age 57, had had an attack of sharp epigastric pain two years previously since which time he had been fairly free of symptoms until ten days before admission when he again had cramp-like epigastric pain three or four times daily. Eight days ago he noted jaundice and clay colored stools and pruritus. He had lost 15 pounds in weight.

Physical Examination.—A deeply jaundiced, poorly nourished man with a normal temperature. The edge of the liver was firm and smooth and 5 cm. below the right costal margin. The gallbladder was questionably palpable.

Roentgenographic Examination.—The gallbladder failed to visualize with dye. A gastro-intestinal series showed the second portion of the duodenum to be irritable but was otherwise normal.

Laboratory Data.—The urine was deeply bile stained. Red blood cells, 4,500,000; hemoglobin, 96 per cent; white blood cells, 6,700; icteric index, 100. All stools were strongly positive for occult blood.

Operation.—Cholecystogastrostomy. The gallbladder was greatly dilated and free of stones. The common duct was also dilated. At the ampulla of Vater there was a firm, movable mass, 1 cm. in diameter. The regional nodes were questionably involved. The pancreas was not involved.

Course.—The jaundice cleared and the patient was discharged greatly improved. He is known to have been gaining weight and feeling well eight months after operation.

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MORTALITY FACTORS IN APPENDICITIS WITH PERFORATION

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THIS paper embraces an analysis of 1,251 cases of appendicitis, complicated by peritonitis and abscess formation, from the Los Angeles County Hospital, Unit 1, during the period from July, 1921, to July, 1935. This study was undertaken with the hope that information of definite value might be obtained regarding the influence of various factors upon the mortality rate.

Any classification must, of necessity, be somewhat arbitrary especially in drawing a distinction between the various grades of peritonitis other than that of definite abscess formation. An attempt was made to exclude complicated cases, unless they were incident to perforation, in order to better evaluate the results of treatment in the face of gross peritoneal soiling, although it is realized that in some cases this is not possible.

The relative incidence and mortality rate are illustrated in the following statistics from this institution. During the ten year period from July, 1925, to July, 1935, there were 7,651 cases of acute appendicitis with a mortality rate of 4.2 per cent. Of these, 1,044 were perforated with a mortality of 26 per cent. Excluding this group, there were 6,607 cases with a mortality rate of 0.78 per cent. That statistics from a relatively small number of cases may be misleading is illustrated in a series of 200 consecutive cases taken from the total group analyzed in detail in which the mortality rate was 8 per cent, approximately one-third of what it was for the total series.

In this series of 1,251 cases, there were 295 fatalities, a mortality rate of 23.5 per cent (Table I).

TABLE I

	Number of Cases	Deaths	Mortality Rate
Cases operated upon.....	1,186	252	21%
Cases without operation...	65	43	66%

Age.—That age has a definite effect upon the incidence, pathologic change, complications, and mortality rate of acute appendicitis is unquestioned. Maes[2] stresses the fact that, in older subjects, appendicitis is fundamentally a vascular disease in which the primary pathologic change tends to be a massive variety of gangrene as the circulation of the appendix is terminal and lends itself especially well to this type of pathology. In this series the incidence after 40 was 21.5 per cent, the mortality rate was 41.8 per cent, and the group accounted for 39.9 per cent of the entire number of fatal cases (Table II).

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TABLE II

THE MORTALITY RATE ACCORDING TO AGE

Decade	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
No. of Cases	146	359	284	190	129	86	37	26	2
Mortality Rate	23%	17.5%	12.6%	23.1%	34.1%	38.6%	67.5%	81%	100%

Sex.—There were 921 males and 330 females. The mortality rate was 21.8 per cent for the males and 28.5 per cent for the females. In the female, the difficulty of distinguishing between peritonitis from appendicitis and acute pelvic inflammatory disease, the greater frequency of obesity, and the occasional complication of pregnancy may account in part for the greater mortality rate.

Duration of Illness Before Operation.—The abscess and diffuse peritonitis groups are tabulated separately, as they show marked differences in the mortality rate for various periods. In the diffuse peritonitis group—peritonitis that has spread beyond a local process variously classified as spreading, diffuse, or generalized—the lowest mortality rate occurred in those operated upon within the first 24 hours; during the next 24 hours, there was a sharp rise and beyond that a steady increase in the death rate until the fourteenth day was passed with only a slight decrease for the third week. It is evident from a study of this group that perforation of an appendix in less than 12 hours does occur and under the 24 hour period is relatively frequent; that operation performed under the 24 hour period in diffuse peritonitis gives the lowest mortality rate and for each succeeding day of delay the mortality rate increases. There were 35 cases of diffuse peritonitis in which operation was not performed, with 27 deaths, a mortality rate of 75 per cent. Of 23 cases in this latter group, in which the duration of the disease was known, 13 died during the first week, seven during the second week, and three during the third week. One patient died on the second day (Table III).

TABLE III

MORTALITY RATE IN RELATION TO DURATION OF DISEASE

Diffuse Peritonitis Group

Day	1st	2nd	3rd	4th	5th	6th	7th	8th–14th	15th–21st
No. of Cases	81	274	174	71	34	16	17	20	5
Mortality Rate	11.1%	27%	28%	32.4%	44%	44%	53%	65%	60%

It would seem evident that, in this locality at least, a truly diffuse peritonitis is a highly fatal disease and once the peritoneal involvement has become widespread, its usual course is progression of the pathologic process and the greatest chance of avoiding a fatal issue lies in prompt and judicious surgical intervention.

In a study of the abscess group, it was found that the lowest mortality rate occurred in those operated upon during the seventh and eighth day period. After this period, the mortality rate rapidly increased to 100 per cent for those of a duration in excess of one month. The highest mortality rate for the first week occurred during the fourth day. From a consideration of these

facts, it seems justifiable to conclude that operation during the first 48 hours of abscess formation gives a comparatively low mortality rate. Operation during the formative period from the third to sixth and especially the fourth day of abscess formation is fraught with danger because the infection has gained virulence over that of the first days and the abscess has not had time to become sufficiently well walled off to make surgical intervention safe. Generally speaking, the seventh and eighth day period is the optimum time for operation. At this time, the abscess is usually well formed and time enough has not elapsed for the development of late complications (Table IV).

TABLE IV

MORTALITY RATE IN RELATION TO DURATION OF DISEASE

Abscess Group

Day	1st–2nd	3rd	4th	5th–6th	7th–8th	9th–14th	15th–21st	22nd–28th	Over 1 mo
No. of Cases..	42	40	34	50	41	58	15	4	6
Mortality Rate	4.7%	15%	26.4%	12%	2.2%	13.7%	40%	75%	100%

The Use of Cathartics.—Almost without exception, authors agree that purgation is an important factor in increasing the mortality rate of acute appendicitis. As Miller[3] emphasized, it is an accessory to delay. That it increases the severity of the pathologic process and hastens perforation seems certain. One thousand cases in this group were studied with reference to the use of cathartics. It was found that in 381 cases a cathartic had been given. The mortality rate for this group was 23.9 per cent. In 141 cases a history of repeated purgation was obtained, in which group 40 deaths occurred, a mortality rate of 28.3 per cent.

Atypical Symptoms and Physical Findings.—Atypical symptoms and signs contribute to delay, and delay favors an increased mortality rate. In this study the following conditions contributed to atypical symptomatology: (1) The pelvic appendix, which is rather common, not infrequently gives atypical and misleading symptoms; left lower quadrant or suprapubic pain is not infrequent, radiation of the pain to one or both testicles or the penis is not uncommon; hematuria, dysuria, diarrhea, tenesmus, or relief of pain on bowel movement may occur. (2) The high retrocecal appendix often causes pain and tenderness in the right costovertebral angle or along the right costal margin and right upper quadrant. (3) The unrotated cecum pointing to the left with the appendix in the left iliac fossa gives left lower quadrant pain and tenderness. (4) The retroperitoneal appendix may give symptoms quite atypical, as pain and tenderness in the groin, right lumbar and costovertebral region or, as in one case, the right lumbar region and back, which radiated to the right shoulder and hip. Another was characterized by pain in the right chest and orthopnea. Pain in the region of the shoulder blades occurred in another in which the cecum, having failed to descend, lay in the right upper abdomen just below the liver with the appendix bound firmly to the posterior abdominal wall. (5) Appendicitis coincident with an incarcerated or strangulated right inguinal hernia in which the presence of the

incarcerated hernia overshadows the symptoms of appendicitis. (6) Cases of pelvic peritonitis in females may confuse the diagnosis between acute appendicitis with perforation and acute pelvic inflammatory disease. (7) First symptoms other than pain. Because an attack of appendicitis almost always begins with pain as the first symptom, a case may be considered atypical and is often confusing if another symptom precedes it. In the first 1,000 cases of this series, there were 62 cases in which the first symptom was one other than pain. There were 25 deaths, a mortality rate of 40.3 per cent. (8) There were 55 cases in which rigidity was absent with 16 deaths, a mortality rate of 29 per cent. Rigidity is not infrequently absent in the obese patient and in the extremes of life.

Location of the Appendix.—It was thought that a study of the location of the appendix in relation to the mortality rate might be interesting and instructive. The retroperitoneal appendix gives a high mortality rate because of the poor resistance of the retroperitoneal tissues and the large size which abscesses in this region are prone to develop with symptoms which are confusing and atypical (Table V).

TABLE V

LOCATION OF THE APPENDIX

First 1,000 Consecutive Cases	Mortality Rate 21.8% No. of Cases	Mortality Rate
Retrocecal appendix	212	18.8%
Pelvic appendix	121	19.8%
Retroperitoneal appendix	14	43 %
Appendix toward midabdomen	12	8.3%
Appendix in left iliac fossa	3	0%
Remaining group	638	23 %

Diffuse Peritonitis.—In this group there were 741 cases with 233 deaths, a mortality rate of 31.44 per cent.

TABLE VI

CAUSE OF DEATH IN 233 CASES OF DIFFUSE PERITONITIS

1. Generalized peritonitis	198 cases	10. Pyemia with multiple liver abscesses, subhepatic and pelvic abscesses	1 case
2. Intestinal obstruction	11 cases	11. Postoperative intraperitoneal hemorrhage, intestinal obstruction and pelvic peritonitis	1 case
3. Localized peritonitis	4 cases	12. Left cerebral capsule embolism	1 case
4. Subphrenic abscess	3 cases	13. Disruption of wound and bronchopneumonia	1 case
5. Pylephlebitis	3 cases	14. Diabetes mellitus	1 case
6. Bronchopneumonia	3 cases	15. Chronic nephritis and uremia	1 case
7. Subhepatic abscess	2 cases		
8. Pulmonary embolism	2 cases		
9. Lobar pneumonia	1 case		

Inasmuch as 85 per cent of the deaths in this group were due directly to generalized peritonitis, our major consideration is the prevention of the

fatal toxemia from widespread peritoneal involvement. In the presence of a widespread peritonitis, there are two factors which are potentially lethal. With every widespread peritoneal involvement, a variable degree of ileus is present and, to a large extent, the severity of the ileus indicates the gravity of the patient's condition. When the peritoneum is subjected to abnormal stimulation, inflammatory and bacterial in the case of peritonitis, or mechanical in an operative procedure, the inevitable response is the development of ileus. When operating in peritonitis it is necessary to reduce manipulative procedures to a minimum not only to avoid spread of peritonitis but also to avoid unnecessary trauma which favors ileus. An advanced ileus is quite similar in effect to an advanced mechanical obstruction. The second potentially lethal factor in peritonitis is the spread of the infection over a wide peritoneal area which increases toxemia from transperitoneal absorption. Its effect on the production of ileus has already been mentioned.

It is difficult to overestimate the value of the Levine tube with suction in combating ileus by reduction of intra-intestinal pressure through decompression of the bowel. The author's opinion is in accord with many others who feel that its value so far outweighs that of enterostomy in the treatment of paralytic ileus that there really is no comparison.

It is remarkable what diversity of opinion exists at the present time in regard to the indication and type of case suitable for deferred operation. From a study of the present series, it seems that the cases herein listed as diffuse peritonitis were, in the overwhelming majority of cases, very definitely of the severe type with little tendency toward subsidence or localization. The tabulated statistics, in this study, bear out this assumption. Furthermore, in a careful study of these case records, the operative and autopsy reports showed that in a fair percentage of cases the peritoneal contamination through the perforation was so gross that nothing short of an overwhelming infection with a fatal issue could be expected unless the source of the infection was removed. For example, there were 11 cases in which the appendix had not been removed at operation, that showed gross fecal leakage from the perforated appendiceal base at autopsy. At operation, in ten other cases, the appendix was found completely sloughed from the cecum, not to mention the cases in which death occurred without operation that showed fecal soiling.

It is difficult to tell with any degree of certainty the case which will eventually subside and localize or go on to an overwhelming and fatal infection. In any large series of cases, however, there will be definite indications for deferred operation with supportive treatment. This applies particularly to the group that appears too sick to withstand a surgical procedure. It must also be admitted that, with increasing experience, a surgeon may widen the field of application for deferred operation with a reduction in his death rate.

It is considered not only advisable but imperative, wherever possible, to remove the appendix when operating for diffuse peritonitis in order to remove the source of peritoneal contamination. This should be the primary

reason for operation. Incision and drainage alone is of doubtful value and offers a poor chance of recovery (Table VII).

TABLE VII

MORTALITY RATE IN RELATION TO OPERATIVE PROCEDURE IN DIFFUSE PERITONITIS

	No. of Cases	Deaths	Mortality Rate
Appendicectomy and drainage	619	153	24.7%
Drainage only	82	49	59.7%
Without operation	40	31	77.5%

It is believed that the McBurney incision, placed well out to the right, close to the anterior superior iliac spine, is attended with a much lower mortality rate in diffuse peritonitis because it offers direct access to the site of the appendix with a minimum of intraperitoneal manipulation and trauma Table VIII).

TABLE VIII

MORTALITY IN RELATION TO TYPE OF INCISION IN DIFFUSE PERITONITIS

	No. of Cases	Deaths	Mortality Rate
Right rectus incision	394	140	35.5%
McBurney incision	140	28	20 %

Type of Anesthesia.—Generally speaking, ether is probably the safest anesthetic for cases of appendicitis complicated by peritonitis as shown by the result for all groups. The mortality rate in this series where spinal anesthesia was used was 5 per cent higher than for ether. However, the author cannot but feel that there is a definite indication for the use of spinal anesthesia in the case where ileus plays a dominant rôle. Another type of case in which a spinal anesthetic is of great advantage is in the obese patient.

ABSCESSES.—There were 320 cases in this group with 54 deaths, a mortality rate of 16.8 per cent. One reason for this high death rate is the fact that a fair percentage of the fatalities occurred in patients with huge abscesses who were in a very critical state when first admitted to the hospital. The long duration in some cases was responsible for the advanced pathology. One case gave a history of six months' duration; six, a duration of one month; and 25, a duration of two weeks or more (Table IX).

Here again generalized peritonitis leads the list as a cause of death. These cases were analyzed in an effort to determine the factor which caused the fatal generalized peritonitis. There were five cases in which it was evident that the operative procedure precipitated the peritonitis due to technical errors in which the abscess wall was invaded from the general peritoneal cavity with dissemination of the infection, two of which were from misplaced, high,

right rectus incisions. Two cases, in which the appendix had not been removed, showed gross fecal leakage from the base at autopsy. In five cases spontaneous rupture of the abscess had evidently taken place previous to operation with the development of generalized peritonitis. In one case following drainage of a pelvic abscess, the patient did well until the ninth postoperative day, when the wound was probed by an intern with resulting peritonitis and death on the twelfth postoperative day. In two cases spontaneous rupture occurred while under conservative Ochsner treatment with resulting peritonitis and death (Table IX).

TABLE IX

CAUSE OF DEATH IN 54 CASES OF ABSCESS

1. Generalized peritonitis	23 cases
2. Appendiceal abscess	7 cases
3. Retroperitoneal abscess	6 cases
4. Intestinal obstruction	4 cases
5. Subphrenic abscess	4 cases
6. Pylephlebitis with multiple liver abscesses and mesenteric thrombosis	3 cases
7. Pelvic abscess	2 cases
8. Retrocecal abscess	1 case
9. Postoperative traumatic wound rupture and postoperative hemorrhage	1 case
10. Bronchopneumonia	1 case
11. Erysipelas	1 case
12. Pulmonary tuberculosis	1 case

TABLE X

MORTALITY IN RELATION TO OPERATIVE PROCEDURE IN ABSCESS CASES

	No. of Cases	Deaths	Mortality Rate
Appendicectomy with drainage	186	20	10.7%
Drainage only	118	24	20.3%
Without operation	16	10	62.5%

It is believed that the appendix should be removed in all cases where it is accessible and can be accomplished without danger of breaking through the abscess wall. This procedure is deemed advisable not so much because of the lower mortality rate shown in this series, as the cases of drainage only were in many instances the more desperately ill, but also because when the appendix is not removed, it is always a potential source of peritoneal contamination even in an apparently walled off abscess.

The most frequently used incisions, the right rectus and McBurney, gave mortality rates which closely approximated, 17 and 16 per cent respectively. The important consideration is to place the incision over the abscess in order that the approach may be direct and contamination of the general peritoneal cavity avoided (Table XI).

TABLE XI

MORTALITY IN RELATION TO TYPE OF INCISION IN ABSCESS CASES

	No. of Cases	Deaths	Mortality Rate
Right rectus incision	151	26	17.2%
McBurney incision	62	10	16.1%

LOCAL PERITONITIS GROUP.—There were 190 cases of local peritonitis with eight deaths, a mortality rate of 4.2 per cent (Table XII).

TABLE XII

CAUSE OF DEATH IN EIGHT CASES OF LOCAL PERITONITIS

1. Generalized peritonitis ..... 5 cases
2. Postoperative intestinal obstruction ..... 1 case
3. Local peritonitis ..... 1 case
4. Pulmonary embolism ..... 1 case

Special mention will be made of the cases of generalized peritonitis in this group. Two of the cases were closed without drainage. While it cannot be positively stated that lack of drainage was responsible for the development of generalized peritonitis, certainly, if the local process was of sufficient virulence to develop a generalized process after removal of the appendix, drainage was indicated in order to expedite a walling off process. One case followed severe intraperitoneal trauma in the form of breaking up of adhesions and removal of mesenteric nodes. Another case, admitted with signs of a definitely localized pelvic peritonitis, was diagnosed and treated as an acute pelvic inflammatory disease, and died of generalized peritonitis without operation. The case which died of local peritonitis was moribund on admission. Autopsy showed a localized fibrinopurulent peritonitis with gross contamination of the pelvis. The case in which intestinal obstruction was responsible for death is interesting because it was a case without drainage.

Intestinal Obstruction.—This includes only the cases of mechanical obstruction. Cases of paralytic or adynamic ileus are considered under generalized peritonitis. There were 31 cases of intestinal obstruction, representing an incidence of 2.4 per cent, with 16 deaths. Inasmuch as there has been much controversy recently concerning the part played by drainage material in the peritoneal cavity as a cause of intestinal obstruction, these cases were studied with particular reference to etiologic factors. There were 21 cases in which there was definite evidence that drains were not responsible. Of these, seven were nondrainage cases. Four others were preoperative obstructions coincident with the development of peritonitis. The others in the group for the most part were obstructions, the result of adherent loops in the wall of the abscess. Two, however, were angulated loops of ileum adherent to the abdominal scar. In nine of the remaining ten, the majority were either cases of generalized peritonitis or localized abscesses in which the exact mechanism by which the obstruction was produced could not be definitely

determined but there were no findings which directly suggested that drains were responsible. There was one case in which it appeared that the drain was the offending factor. At autopsy it was shown: "In the iliocecal region is a thickened inflammatory mass through which passes a Penrose drain, extending part way to the pelvis. In this inflammatory mass are incorporated several of the terminal loops of the ileus which are markedly collapsed."

Intraperitoneal Drainage.—In this series, intraperitoneal drainage was the rule. There were 50 cases, however, without drainage and they were almost exclusively cases of local peritonitis. There were four deaths. Two were due to intestinal obstruction, one of which occurred with a secondary abscess following local peritonitis. The other two fatalities were due to generalized peritonitis. In those drained, the drainage material in nearly all cases consisted of the soft rubber tissue Penrose type.

Drainage is a valuable adjunct in treatment but it has definite limitations and too much must not be expected of it. In the first place it must be realized that a drain in the peritoneal cavity becomes walled off in a comparatively few hours, and for that reason it is obviously impossible to drain any large part of the peritoneal cavity for any protracted period of time. The indication for drainage of an abscess is universally accepted.

That the peritoneum may be unable to cope successfully with local peritonitis, following removal of the source of peritoneal contamination, was well illustrated in two fatal nondrainage cases in this series in which generalized peritonitis developed. It seems that drainage in local and early peritonitis is definitely indicated, for here by the use of drains the involved area is more apt to be isolated and walled off. Drains are especially indicated if raw or oozing surfaces are left, particularly if the appendix is embedded in the wall of the cecum or retroperitoneal tissues. The use of drains under such circumstances have a tendency to reverse the lymphatic current and augment the natural defensive powers. Thus the incidence of widespread peritonitis and abscess formation will be decreased. Although secondary abscesses may develop even though drains are used, they are not as frequent and not as pernicious when they do.

The value of drainage in diffuse peritonitis is distinctly limited. When the appendix is not removed, drainage of the focal area may help wall off the source of infection from the general peritoneal cavity. With pus under great tension and intraperitoneal pressure increased, drainage relieves tension, temporarily at least, and reduces transperitoneal absorption for a short time.

For intraperitoneal drainage, rubber tissue drains of the Penrose type should be used, as hard material, such as stiff rubber tubes, may cause necrosis of adjacent tissues, and trauma favors the formation of dangerous adhesions. In order to avoid the possibility of intestinal obstruction, it is important to place the drains in such a manner that they lie in contact with the parietal peritoneum and do not pass between intestinal coils.

Enterostomy.—The nature of diffuse or generalized peritonitis is such

that frequently it is impossible to distinguish clinically between paralytic and mechanical ileus. This is true in a large measure because often the pathologic condition is a combination of mechanical and paralytic factors. When such a condition obtains, the paralytic factor is often dominant to the extent that an enterostomy does not function during the critical period, that is, during the first two or three days postoperatively. However, an enterostomy in cases with a peritonitis, and in the presence of a definite obstruction, may be a life saving operation by relieving the obstruction with a minimum of intraperitoneal manipulation. Not infrequently the relief is permanent because with the subsidence of the inflammatory process the obstruction is relieved.

By using the Levine tube with continuous suction, there are many cases which may be tided over the critical period that formerly we would have operated upon. It is possible to keep the small bowel fairly well decompressed by this method and may save the patient a secondary operation for the relief of postoperative ileus when the mechanical factor is not complete.

Ileostomy was used in 15 cases of paralytic ileus with 12 deaths, and in nine cases of mechanical ileus with eight deaths. As a primary procedure it was used in 15 cases with 11 deaths, a mortality rate of 73.3 per cent, and in nine as a secondary procedure with nine deaths.

Colp,[1] in writing of enterostomy in ileus, reported nine cases in which enterostomy was performed for acute appendicitis with general peritonitis. There were seven deaths. In 21 cases in which enterostomy was performed in paralytic ileus incident to general peritonitis, the mortality rate was 85 per cent. He concluded that ileostomy as an aid in relieving intestinal toxemia had little to offer and that enterostomy had no indications in the paralytic type of ileus.

Treatment of the Appendiceal Stump.—Apparently it makes little difference whether the appendiceal stump is inverted or simply tied and dropped. There are many instances in which inversion is not practical because the surrounding cecal tissue is too friable. In case the adjacent cecum is necrotic and gangrenous or the appendix is sloughed, leaving a hole, the quickest, and probably the safest, procedure is to perform an appendicostomy. In three cases, without inversion of the stump, gross fecal contamination occurred and was undoubtedly the cause of death, one case being accompanied by intraperitoneal hemorrhage. In two cases, with stump inversion, gross leakage occurred followed by death from general peritonitis.

CONCLUSIONS

(1) The treatment of acute perforated appendicitis constitutes a real challenge to the judgment and technical ability of the well trained surgeon.

(2) The mortality rate for diffuse peritonitis increases rapidly from the second to the fourteenth day. In the abscess group the mortality rate is lowest for cases operated upon during the seventh and eighth day period.

(3) Deferred operative treatment has definite indications but is a hazardous procedure except in experienced hands.

(4) Generally speaking, it is believed that the procedure of choice in appendicitis with peritonitis is operation after a reasonably brief period of preoperative preparation.

(5) Removal of the appendix should be effected whenever possible without too much intraperitoneal trauma.

(6) The McBurney incision should be the incision of choice for appendicitis with peritonitis.

(7) Proper intraperitoneal drainage should decrease the mortality rate for all types of appendicitis with perforation. Proper drainage apparently does not favor the development of intestinal obstruction.

(8) Appendicostomy may be used to advantage in certain instances in order to avoid fecal leakage from a necrotic and gangrenous appendiceal stump.

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SQUAMOUS CELL CARCINOMA OF THE LOWER RECTUM AND ANUS *

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Squamous cell carcinoma arises not uncommonly in the lower rectum and anus. It has many interesting features. It occurs more frequently among females than among males. Chronic irritation is suspected to play an important part in its origin. Pain is sometimes an early symptom. Metastases rarely spread upward above the pelvic peritoneum or more distant than the groin. The primary tumor is relatively radiosensitive. It forms, apparently, a distinct clinical entity, and differs from adenocarcinoma of the rectum in important respects. The treatment of the two diseases is accordingly different.

The material herein considered consists of 27 proven cases, all with microscopic confirmation of the original diagnosis. For the sake of comparison, a series of adenocarcinomata of the rectum has been worked out in their essential detail.

Incidence.—The incidence of squamous cell carcinoma of the lower rectum and anus was 5.7 per cent. The cases occurred in a series of 470 cases of carcinoma of the rectum and anus of all types. Buie and Brust[2] reported an incidence of 1.7 per cent; Raiford,[17] 2.8 per cent; Funke,[5] 3 to 4 per cent; and Quénu,[16] 20 per cent.

In the anus excluding the rectum, there were 18 cases of squamous cell carcinoma and 17 cases of adenocarcinoma. These figures were deducted from a study of 70 cases of anal carcinoma at the Barnard Free Skin and Cancer Hospital. Of the 70 cases, microscopic sections were available in 35 cases, and not available in 35 cases.

Sex.—There were 23 females and four males. So few males had the disease that some etiologic factor preponderant in the female sex was suspected. Raiford remarked upon the high incidence among the females of his series: namely, eight females to two males. Buie and Brust, however, noted a distribution more equal: 25 females to 22 males.

Age and Race.—The average age of the patients of this series was 57 years, three years older than those with adenocarcinoma of the rectum. This is the same as the average age of Buie and Brust's patients, but higher than that of Raiford's (48.7 years), and higher than that of Rosser's[20] (51 years). The youngest patient of this series was 27 years old; the oldest,

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79. There were 21 whites and six Negroes in this series. Raiford recorded eight whites and two Negroes.

Concomitant Local Factors.—Local irritation about the anus was rarely absent at the time of onset of the disease. Hemorrhoids or condylomata were present in seven instances; fistula-in-ano or abscess in five. Three patients noted leukorrhea. Unusual trauma to the anus occurred once from sodomy and once from a fall. Syphilitic condylomata were associated once. Benign stricture of the rectum in a Negress with a positive Frei reaction preceded the disease in one instance. Operations such as hemorrhoidectomy, local excision, *etc.*, had been performed previous to admission in ten cases.

Squamous cell carcinoma of the anus occurred after squamous cell carcinoma of the vulva in two instances.* One of these anal carcinomata (Barnard Hosp. No. 42327) developed in an area of peri-anal leukoplakia seven years after operative treatment and apparent cure of the vulvar carcinoma. The other anal carcinoma (Barnard Hosp. No. 22009) arose in a peri-anal scar resulting from treatment and apparent cure four years previously of a vulvar carcinoma by means of application of radium.

Symptomatology.—Symptoms in squamous cell carcinoma of the lower rectum and anus had been present on the average 18 months at the time of admission, which was five months longer than for adenocarcinoma of the rectum. The shortest duration of symptoms was three weeks, the longest three years.

Squamous cell carcinoma seemed to cause pain as a frequent and early symptom. The pain was due probably not to the carcinoma itself, but to fissure of the anal mucosa or to associated infection. Pruritis was also a common and early symptom, as was bleeding. Some patients felt an unusual mass in the anus. Pus and pain on defecation were also fairly common. Sometimes change in bowel habit was noted, with either constipation or diarrhea, or with both in alternation. Ribbon or pencil stools were passed at times, and some stools contained blood or pus. In the later stages, frequency or urgency of urination was noted. Other symptoms were incontinence of feces, perirectal abscess, and fistula-in-ano. Some patients lost weight. A few noted a mass in the groin.

The symptomatology was not characteristic of the squamous cell type of carcinoma. Similar symptoms were also noted in the presence of adenocarcinoma of the anus. Rosser observed that "pain was the predominant and presenting symptom in 60 per cent . . . [of his cases of anal carcinoma]. The absence of definite constipation in 76 per cent of the cases was a surprising observation."

Objective Physical Phenomena.—All tumors of this series were readily accessible to the examining finger, and some of them were visible from the outside, and had been noticed by the patients themselves. Eight of the

* These two patients are included in the series by the kind permission of Dr. Frederick J. Taussig.

tumors were externally situated, 11 internally situated, some running high into the rectum; the situation of the remainder being unspecified. The highest tumor (Jewish Hospital No. 340401) extended 8 cm. above the anal orifice. The average diameter was 4 cm., the extremes being 1 x 2 cm. and 6 x 7 cm. One tumor only was annular (Barnes Hosp. No. S-5027), the remainder being discrete, or of unspecified extension. In this respect squamous cell carcinoma did not resemble adenocarcinoma, which latter not infrequently encircled the anal canal in annular fashion.

Five of the tumors originated posteriorly, two laterally, and one anteriorly, the remainder, excepting the one annular tumor, being unspecified in site. The apparent anterior origin of the one tumor (Barnes Hosp. Nos. S-10980, S-12392) was unusual. Buie and Brust state that "the posterior half of the anal wall seems to be more commonly involved by all lesions, and we have found no exception to this rule."

Fourteen tumors were ulcerative, nine papillary, the rest being undescribed in this respect. In general, the ulcerative type was the more malignant, and microscopically was less well differentiated.

The characteristic appearance of carcinoma was rarely lacking upon inspection or palpation of any of the tumors. Usually the border was raised, pearly, irregular, with an underlying sense of induration and often fixation. Some tumors were friable and bled easily. Some were enormously heaped up. Others burrowed through the sphincters, into the ischiorectal fossae, with multiple fistulae or abscess formation. Signs of cachexia were sometimes present.

Biopsy was employed to confirm the diagnosis in most instances. If not taken before treatment, section of the operative specimen was always performed for microscopic confirmation. Without biopsy, adenocarcinoma could not be ruled out.

The more common errors in diagnosis previous to admission, or on admission, were hemorrhoids, fistula-in-ano, perirectal abscess, simple ulcer or fissure.

Metastases.—The character of metastatic spread of squamous cell carcinoma of the lower rectum and anus is illustrated in Table I. Twenty-three of the 24 instances of metastases were in the downward or in the lateral zones of Miles,[14] or in the inguinal lymph nodes. The general direction of metastatic extension seemed, therefore, to be downward and lateral but not upward.

By contrast, the general direction of metastatic extension of adenocarcinoma seemed upward rather than downward and lateral. There were in the group of adenocarcinomata, 24 instances of metastatic deposits in the upward zone of spread and in the liver, as compared with 19 instances of metastatic deposits in the downward and lateral zones and in inguinal nodes.

It seems desirable to amplify the description of the metastatic spread of the squamous cell type of carcinoma because of its important bearing upon the operative treatment of the disease. The thesis that metastases from

squamous cell carcinoma of the lower rectum and anus are usually rather well circumscribed and rarely distant, has not previously been clearly set forth. Furthermore, the failure of squamous cell carcinoma of the lower rectum and anus to spread in the upward zone of Miles is believed to be an original observation, and thus requires amplification also. As a working basis, the classification of Miles for spread of adenocarcinoma has been used and applied to squamous cell carcinoma.

TABLE I

METASTASES

Metastases	Squamous Cell Carcinoma of Anus	Adeno-carcinoma of the Rectum
Zone of Spread (after Miles[14])		
(1) Downward	12	5
(Peri-anal skin, ischiorectal fat and external sphincter muscles)		
(2) Lateral	9	11
(Lymphatics of levator ani and coccygeus muscles, prostate, pelvic peritoneum, base of bladder, cervix uteri, broad ligaments)		
(3) Upward	0	14
(Lymph nodes of retrorectal or lowermost mesocolic region, of pelvic mesocolon, paracolic nodes, left common iliac node, median lumbar node)		
Liver	0	10
Inguinal lymph nodes	4	3
Lungs	1?	0
Bone	0	2
Total metastatic foci	26	45
Total patients with metastases	19	25

(1) DOWNWARD ZONE OF SPREAD. Miles defines this zone as the "peri-anal skin, the ischiorectal fat, and the external sphincter muscle." Squamous cell carcinoma invaded this zone in 12 out of 19 patients with metastases. The peri-anal skin and external sphincter muscle was infiltrated with carcinoma in ten cases, with extension to the ischiorectal fossa in four of them. The downward zone was found free of metastatic involvement in only three of the 15 operative surgical specimens examined. Involvement of the downward zone by squamous carcinoma, therefore, was quite common.

Involvement of the downward zone by adenocarcinoma was, by comparison, considerably less common; and occurred only five times as compared to ten times for squamous cell carcinoma.

(2) LATERAL ZONE OF SPREAD. Miles defines this zone as the "lymphatics of the levator ani and coccygeus muscles, the pelvic peritoneum, the

prostate gland, the base of the urinary bladder, the cervix uteri, and the base of the broad ligament." Squamous cell carcinoma invaded this zone in nine out of 19 patients with metastases. The lymphatics of the levator ani and coccygeus muscles contained metastatic deposits in five instances, the pelvic peritoneum was invaded once, the capsule of the prostate once, and the cervix uteri twice. Involvement of the lateral zone by squamous cell carcinoma, therefore, was only slightly less common than involvement of the downward zone.

For adenocarcinoma, by way of contrast, involvement of the lateral zone was somewhat more common than for squamous cell carcinoma, with 11 cases of adenocarcinoma to nine of squamous cell carcinoma.

(3) Upward Zone of Spread. Miles defines this zone as the "rectorectal (lowermost mesocolic) nodes, the pelvic mesocolon in its entirety, the paracolic nodes, the nodes situated at the bifurcation of the left common iliac artery, and the median lumbar (aortic) nodes." This zone was not invaded by metastases from squamous cell carcinoma of the lower rectum and anus in this series. The evidence for freedom of this zone from metastases was the result of the observations of surgeons at celiotomy on 12 of the patients of the series, confirmed by biopsies in two instances. In addition there was one necropsy.

ILLUSTRATIVE CASE REPORTS

Case 1.—A white housewife, age 50 (Barnes Hosp. No. S-5027), was admitted January 23, 1918. Patient had had diarrhea, tenesmus, and bleeding per rectum for one year. Examination revealed an infiltrating carcinoma of the left and anterior sides of the anus, extending up the anus into the rectum for a distance of 8 cm. The tumor involved the skin, external sphincter muscle, vaginal wall, and ischiorectal fossa with fistula formation. The groins were not suspicious of metastases. Microscopically the tumor was a relatively undifferentiated squamous cell carcinoma. Operation January 30, 1918. Perineal excision of anus and rectum, 14 cm. of gut being excised with some of the vaginal wall; perineal colostomy. Death from sepsis, February 10, 1918. The gross specimen showed metastatic involvement of the highest lymph node of the specimen. (Note: this was the highest point reached by metastases from squamous cell carcinoma of the lower rectum and anus in this series.) Necropsy (No. 959) showed wound infection, pelvic peritonitis, acute cystitis, and acute splenic tumor. No metastases or evidence of remaining primary tumor were found in the pelvis or abdomen. No metastases in the liver. Microscopic sections negative for carcinoma.

Case 2.—A white housewife, age 50 (Barnard Hosp. No. 56027), was admitted to the hospital November 1, 1933, complaining of cramp-like pain on defecation for the previous two weeks, pain at the anal margin, and blood on toilet paper. Examination showed a hard ulcerated tumor, 3 x 1.5 cm., on left side beginning 3 cm. within anus. Biopsy November 3, 1933, was reported as chronic inflammation. Repeated biopsy November 18 showed squamous cell carcinoma, Grade 2. Operation November 25, 1933. Abdominoperineal excision of anus and rectum, Babcock technic, with perineal colostomy. Exploration through the abdomen during abdominal part of operation revealed small smooth liver, no palpable mesenteric lymph nodes. About 20 cm. of rectum and all of the anus was excised. Fairly wide removal of perirectal and peri-anal tissues; bowel brought down for perineal colostomy. Convalescence uneventful. Symptomatically and clinically well for about two and one-half years. Bowels were rather constipated.

Had warning of impending defecation, but no voluntary control of defecation. Occasional soiling. Occasional incontinence of urine. July, 1935, pain in left leg and sleeplessness. Examination revealed no suspicion of carcinoma, except by digital examination through the perineal colostomy where a mass was felt in the left iliac region. September 27, 1935, a hard mass was felt which extended into the left iliac region beyond reach of the finger. Roentgenologic examinations were negative. Metastasis was suspected, and patient was given high voltage radiation. Course downhill. Chronic intestinal obstruction developed for which patient went to another institution (St. Luke's Hosp. No. 101071). Exploratory celiotomy there June 27, 1936. Obstruction found caused by adhesions pulling ileum into pelvis. Liver small and smooth. The mesenteries contained enlarged lymph nodes. Biopsy taken from one of these. There was a hard mass in the pelvis about the perineal colostomy. Ileostomy performed. Patient died June 30, 1936, of intestinal obstruction; no necropsy. Report of lymph node (St. Luke's Hosp. No. S. P. 14172) biopsy, "hyperplasia; no carcinoma." (Slide personally reviewed and diagnosis concurred in.)

The first of these two cases showed a metastatic deposit at the highest level of any case of this series: namely, just below the reflection of the pelvic peritoneum onto the rectum. This point of metastasis was at the highest part of the zone of lateral spread, and necropsy failed to show extension to the zone of upward spread.

The second of the two cases died presumably as the result of metastasis at about the same level. Biopsy of a mesenteric lymph node taken at a higher level showed no carcinoma. Carcinoma was not demonstrated in the zone of upward spread in this instance. Involvement of the zone of upward spread by squamous cell carcinoma, therefore, was not found in this series, though often sought.

Adenocarcinoma, on the other hand, spread through the upward zone commonly, and 14 such instances were found out of 45 metastatic deposits recorded in the series of adenocarcinoma (Table I). This finding has often been made elsewhere, and is the one upon which Miles has laid great stress as the reason for urging the performance of his relatively radical type of resection, aimed as it is especially to excise the upward channels of lymphatic spread.

The literature does not mention the absence of spread of the squamous cell type of anal and rectal carcinoma through the upward zone. This contribution, if substantiated, may therefore be regarded as original.

Liver. Liver metastases from squamous cell carcinoma of the anus and rectum were not found in this series. Eleven patients with the disease were explored either by celiotomy or at necropsy, and liver metastases were not found in any instance. Adenocarcinoma, on the other hand, metastasized to the liver in ten instances.

Two instances of metastases to the liver from squamous cell carcinoma of the rectum and anus have been found in the literature, one of them reported by Buie and Brust, and another of them by Raiford, who quotes a case of Binkley's. It is interesting to note that both of these cases were said to have received roentgen therapy in the course of the treatment of the anal carcinoma.

Inguinal Lymph Nodes.—Inguinal metastases caused the death of two of the four patients in whom they occurred. The other two patients with inguinal metastases were failing rapidly when last seen.

These metastases sometimes appeared a long time after the disease had originally been treated with apparent cure. For instance, metastases appeared in the left groin of one woman (Barnard Hosp. No. 30465) after an interval of four years of freedom from clinical evidence of the disease; primary treatment had consisted of one stage perineal excision of the anus and rectum with perineal colostomy. The time intervening between the

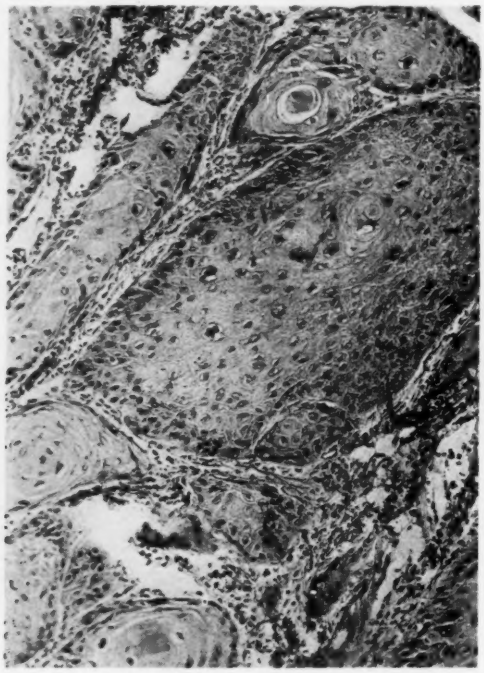

FIG. 1.—Photomicrograph of squamous cell carcinoma of the anus shown in Fig. 2. The tumor is rather well differentiated, and shows pearl formation (Barnard Hosp. No. 62099).

appearance of inguinal metastases in the three other patients was four years, two and one-quarter years, and one and one-third years respectively.

Inguinal metastases were also found from primary adenocarcinoma of the rectum (Table I). There were three instances of it compared to the four cases of squamous cell carcinoma just discussed.

Lungs.—Lung metastases from a squamous cell carcinoma of the anus might have been present in one woman of this series (Barnard Hosp. No. 22009). This patient is reported to have died of lung metastases, but necropsy was not obtained. Moreover, the patient had had a primary carcinoma of the vulva four years previously. No conclusions are to be drawn from this case. The series of adenocarcinomata showed no lung metastases.

Bone.—Bony metastases were not found in the series of squamous cell carcinoma of the lower rectum and anus, although occurring twice in the series of adenocarcinoma of the rectum.

Microscopic Findings.—The microscopic picture of one of the cases of squamous cell carcinoma of the lower rectum and anus is illustrated in Fig. 1. It represents a tumor of the more differentiated type, and resembles the type described by Raiford as discrete. The cells consist of adult horny epithelium, with relatively few mitoses; intercellular bridges are seen, and there is pearl formation (Fig. 1). In the gross these tumors were generally papillary (Fig. 2). There were 11 such tumors in this series.

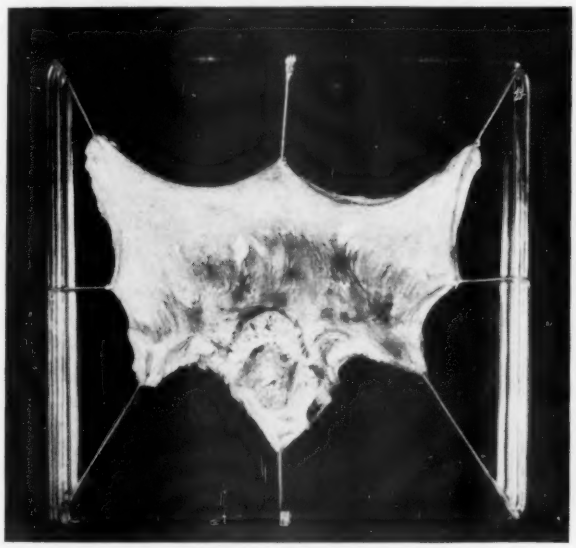

FIG. 2.—(Barnard Hosp. No. 62099.) Gross specimen of squamous cell carcinoma originating on the left side of the mucocutaneous junction of the anus. Male, age 48. One stage perineal excision of anus and rectum up to the reflection of the peritoneum. Permanent perineal colostomy; no abdominal colostomy at any time. Patient clinically well 18 months postoperatively. Has warning of impending defecation, but no control, as sphincters were removed at original operation. Bowels move once daily at 6 A.M.

Fourteen of the tumors of this series were of a less differentiated, more malignant looking type, resembling those described by Raiford as diffuse. The cells of such tumors were smaller with nuclei relatively larger, showing greater degree of pyknosis, absent hornification and more frequent mitotic figures. Most tumors of this type contained broad strands from 10 to 20 cells in thickness penetrating the tissue spaces. Two others in some ways resembled basal cell carcinoma (Barnes Surg. Path. No. 6769; Jewish Hospital Surg. Path. No. 8627). One of the tumors of this group showed a tendency to glandular formation (Barnard Hosp. No. 37035). The two remaining tumors contained elements of both of the two groups above. The microscopic features of the metastatic deposits usually resembled those of

the primary tumor. Graded by Broders' method, five of the tumors of this series were Grade 2, two were Grade 3; the remainder were ungraded.

In considering the question of prognosis, it seemed that gross characteristics furnished a slightly more reliable basis than did microscopic characteristics. However, consideration of all of the characteristics of the individual case was of greater value than reliance upon any one feature alone.

The rate of operability for this series was estimated to be 44.4 per cent. On comparable data, an estimate of the operability of all types of carcinoma of the rectum was 21.4 per cent.

The operative mortality for the series was 12.9 per cent. There were four postoperative deaths and 31 operations. Operations were of six general types.

Type I included local operations. Tissues excised included the tumor and a varying degree of mucous membrane, underlying skin and sphincter ani muscle. There were eight such operations and no deaths.

Type II operations were performed by the perineal approach alone, and without preliminary abdominal operation. Tissues excised included the anus and rectum up to or somewhat above the level of the peritoneal reflection upon the rectum. For exposure the coccyx was always excised, and sometimes the lowest sacral segment in addition. No attempt was made to save the anus. The sphincter ani muscles were always entirely removed, together with some of the coccygeus and levator ani muscles, the contents of the ischiorectal fossae, and a wide margin of peri-anal skin. A permanent perineal colostomy was established by loosening the remaining bowel above the level of excision and bringing it down. Five such operations resulted in one postoperative death.

Type III operations generally resembled the Lockhart-Mummery procedure. An abdominal colostomy of the permanent double barrel type, usually a sigmoidostomy, was performed. At the same stage or at a later stage, the anus and rectum were then excised by the perineal route in a manner usually somewhat more extensive than in Type II, but with no attempt to establish the perineal colostomy. Eight such operations resulted in two postoperative deaths.

Type IV operations included one stage combined abdominoperineal operations for excision of the anus and rectum. The operation was performed after the method of Miles in one instance and of Babcock in two others. Three such operations resulted in no mortality.

Type V operations included dissection of the inguinal and femoral lymph nodes, bilateral operations usually being performed. Six such operations resulted in no mortality.

One operation of unknown nature resulted in postoperative death.

Radiation Therapy.—Two of the primary tumors of this series received radiation, one reacting favorably, the other showing little regression. The latter tumor (Barnard Hosp. No. 19066) recurred after radium treatment,

and was subsequently destroyed by cautery. The patient died of apoplexy after seven years. The history of the first case is as follows:

Case Report.—(Barnes Hosp. No. U-42772.) A white housewife, age 48, was admitted because of severe rectal pain of nine months' duration. She was found to have an ulcerative lesion 1 x 2 cm., high on the posterior anal wall. Biopsy showed squamous cell carcinoma of relatively undifferentiated type without round cell infiltration. Inguinal nodes were not significantly enlarged. On April 7, 1934, under general anesthesia, eight 1.5 millicurie gold radon seeds were implanted into the lesion and about it, total dosage being 12 millicuries. There was severe pain following this treatment. On May 20, 1934, ulceration persisted, but biopsy failed to reveal the presence of any remaining carcinoma. On May 23, 1934, bilateral inguinal and femoral lymph node dissection was undertaken; microscopic examination of the nodes revealed no carcinoma. Patient was readmitted on September 3, 1934, with residual ulcer and fistula-in-ano at site of the original tumor. A resection of both ulcers and fistula was performed; microscopic examination of the tissues revealed no carcinoma. Patient reported well with no sign of recurrence on March 4, 1937.

Radiation was employed for palliative purposes in six instances. In three, roentgen therapy was administered to local recurrences in the pelvis about the site of preceding surgical excision; all three were relieved temporarily, but all died eventually. In the remaining three, roentgen therapy was administered to metastases in the groin, with some resultant improvement, but with eventual death in two cases, and with rapid decline until patient stopped reporting in the third case.

Lacassagne[10] believes that squamous cell carcinoma of the anus tends to leave the realm of surgery in favor of radiation. He refers to two of his eight patients living and well five and eight and one-half years respectively following treatment with radium. Gabriel cites favorable results from the treatment of eight operable cases of squamous cell carcinoma of the anus and anal canal by the use of radium needles. Three of his cases were alive and well up to three years following treatment.

Results.—Twelve patients of the series are known to be dead. Seven died of carcinoma, four postoperatively, and one of apoplexy. Of the seven deaths from carcinoma, four were due to its local reappearance in the perineal wound; two were due to metastases to the groin, and one to questionable metastases to the lungs, unproven by necropsy.

Four patients had carcinoma when last seen. Of these, two had the disease locally recurrent in the perineal wound, and two had inguinal metastases. Five patients were unfollowed. Six patients remain clinically free of the disease at the last examination (Table II).

The rate of five year survival for the disease was 28.6 per cent. Four out of 14 patients treated survived five years or more.

Of the four patients of this series who survived five or more years, three are now dead, and the fourth now has evidence of local recurrence of carcinoma. Of the three dead, one died probably of carcinoma, one possibly of carcinoma, and one probably not of carcinoma but of apoplexy.

TABLE II

PATIENTS CLINICALLY WELL WHEN LAST EXAMINED

Case Number Sex Age	Date of First Operation	Type of Operation	Date Last Examined	Survival Period
54771—Barnard F. 30 yrs.	7- 8-33	(1) Abdominoperineal (Babcock) with perineal colostomy (2) Bilateral inguinal dissection	2-17-37	3 yrs., 7 mos.
340401—Jewish F. 75 yrs.	1-23-34	Perineal excision with perineal colostomy	3- 3-37	3 yrs., 2 mos.
U-42772—Barnes F. 48 yrs.	4- 7-34	(1) Radon 12 millicuries (2) Bilateral inguinal dissection	3- 4-37	2 yrs., 9 mos.
58749—Barnard F. 48 yrs.	8-14-34	Perineal excision with perineal colostomy	4- 6-36	2 yrs., 4 mos.
62099—Barnard M. 48 yrs.	7-26-35	(1) Perineal excision with perineal colostomy (2) Bilateral inguinal dissection	2-17-37	1 yr., 5 mos.
42327—Barnard* F. 66 yrs.	9-24-35	Local excision	2- 9-37	1 yr., 5 mos.

* Patient had had a carcinoma of the vulva excised and dissection of inguinal regions performed seven years previously.

COMMENT.—The disease may prove to be sometimes preventable. Adequate treatment of anal and of certain cervical or vaginal diseases may remove a chronic irritant factor which, if continued, might serve as accessory in giving rise to a carcinoma in the anus. Areas of leukoplakia about the anus are to be observed with suspicion, if not removed. Radiation of the perineum must always be administered with care lest it predispose to carcinoma of the anus.

Since pain seems to be an early symptom of the disease, earlier diagnoses may be expected if examination of the anus and rectum is not neglected.

For an estimate of operability of a given case of the disease, exploratory celiotomy would seem to be an unnecessary adjunct. Information obtained from such an operation may rarely be expected to add anything significant to the local clinical findings, because the metastases from the primary tumor are not directed upwards to the liver.

In treatment of the primary tumor, a choice is to be made between surgery and irradiation, for some of the primary tumors of this type are radiosensitive. It is hardly necessary to recall that adenocarcinoma of the rectum is relatively radioresistant. For the treatment of perirectal metastases, surgery alone, at

present, seems to be the most efficacious procedure. Inguinal metastases have not yet proven amenable to cure either by surgery or by radiation, though they may be prevented by surgery.

Regarding operation, certain principles may be advanced as a result of this study. The primary tumor must be widely excised. For adequate removal, no attempt should be made to conserve the sphincter, and a radical excision of the anus and rectum is to be performed. To be complete, the operation should, in addition, remove a maximum of the tissues in the downward and lateral zones of Miles: namely, a wide amount of the peri-anal skin, the sphincter ani muscles, the ischiorectal fat; together with the coccygei and levator ani muscles and the pelvic fascia and pelvic peritoneum laterally to the pelvic walls.

Dissection, however, need not be carried as high in the zone of upward spread as is advocated by Miles for adequate excision of rectal adenocarcinoma. It would seem adequate in squamous cell carcinoma of the lower rectum and anus to excise the tissues only in the lower part of this zone. Thus it would seem adequate to excise the retrorectal and lowermost mesocolic lymph nodes; and to avoid excision of the entire pelvic (sigmoid) mesocolon as a step needlessly radical. In other words, the optimum height for amputation of the rectum would seem to be a moderate distance above the reflection of the peritoneum upon the rectum.

Amputation of the rectum at this level may readily be performed by the perineal route following the plan of Lockhart-Mummery. This procedure carries, in most hands, an operative mortality which is lower than the mortality from the various types of abdominoperineal excision of the rectum based on the principles of Miles.

Bilateral dissection of the inguinal and femoral lymph nodes must be borne in mind in every case of squamous cell carcinoma of the lower rectum and anus. Squamous cell carcinoma probably will not metastasize to the groin in every case. However, the metastases to the groin almost always prove fatal. Hence, one would seem justified in recommending a so called prophylactic bilateral inguinofemoral lymph node dissection. Such a dissection seems to be a necessary adjunct to the removal of the primary tumor. Raiford, it is true, has advanced objections to this procedure on sound theoretical grounds. Still the procedure remains the best means at present available to prevent the calamity of inguinal metastases.

It is at present unsafe to suppose that established inguinal metastases may be dealt with by surgical excision with hope of such a fair percentage of five year survivals as may be expected in the case of squamous cell metastases to the neck from carcinoma of the lip, mouth, *etc.* Cervical metastases of such nature may be surgically controlled for periods of five years or more in some 33 per cent of cases.

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RUPTURE OF THE SUPRASPINATUS TENDON

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Complete rupture of the supraspinatus tendon is a lesion that has been admirably described in the cadaver,[1,2] and in cases of late shoulder injuries.[3] It has rarely been described soon after rupture occurred.[4,5] During the past year we have seen five patients with this condition within 17 days following injury. Three of them we were fortunate enough to see within three days. We have found the diagnosis of this injury not difficult and its treatment satisfactory. The five patients were operated upon and the rents repaired. In four cases repair was effected within 13 days after the injury. We believe that the lesion occurs not infrequently, as both Codman and Wilson have pointed out, and wish to report our experiences together with a brief résumé of the subject.

Anatomy.—The supraspinatus muscle arises by fleshy fibers from the supraspinous fossa of the scapula. It runs forward and laterally under the trapezius, the acromium and the coraco-acromial ligament to be inserted into the greater tuberosity of the humerus. It is usually about 6 cm. long and the distal tendinous half is inseparable from the capsule of the shoulder-joint. Its insertion is continuous with the insertion of the subscapularis, infraspinatus and teres minor. Together, these form what Codman terms the musculotendinous cuff. The supraspinatus lies superiorly and forms the roof of the shoulder-joint and the floor of the subacromial bursa. Codman has stressed the importance of this relationship.

The action of the supraspinatus is to assist the deltoid in abducting the arm, by pulling the head of the humerus beneath the acromium and preventing the tuberosity from seeking a fulcrum on the acromium or on the coraco-acromial ligament.

Etiology.—Rupture of the supraspinatus tendon is usually found in men past middle age. Codman's patients had an average age of 55.[6] Wilson reported a rupture in a man of 35, the youngest case on record. Our five patients were in the sixth decade of life, the youngest 52 and the oldest 58. All were muscular men who had done laborious work for many years. This bears out the theory that there are pathologic changes in the tendon due to age and occupation that predispose it to rupture.[6] There is normally repeated compression of the tendon against bone when the arm is abducted, and in individuals performing hard work, this factor undoubtedly produces circulatory changes. We know that by decreasing the circulation in any mesenchymatous tissue of low metabolic rate, pathologic calcification may occur,[7]

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and the tendon of the supraspinatus is more frequently affected than any other.[8]

In one of our cases the immediate trauma was slight (Case 3). The man was loading a box of milk bottles on a truck. He had performed this same maneuver for many years and as nearly as he could remember, he handled the box in the usual manner at the time of the accident. In three of the other cases (Cases 1, 2 and 5) the men fell, two said they landed on their shoulders and one stated that he fell on his elbow (Case 2). Codman[6] believes that the rupture occurs from sudden elevation of the arm in attempting to regain balance during a fall, probably before the individual strikes the ground. The fifth patient was struck directly on the shoulder by a falling box (Case 4). This produced the largest tear of the five and has been the only case to present any complication. It is possible that in this man there was an anterior dislocation of the head of the humerus followed by spontaneous reduction.

Pathology.—One of our patients was operated upon five days after injury, two six days, one 13 days and one 70 days. In the four operated upon before the thirteenth day, the rents were immediately proximal to the insertion of the tendon. In each of these cases there were definite stubs of tendinous tissue left attached to the tuberosity. In the case (Case 5) in which 70 days intervened between the accident and the operation, the lesion was similar to those that Codman[6] and Wilson[3] described. The tuberosity was almost bare of tissue and the margins of the tear were smooth.

In three of the cases (Cases 1, 3 and 4), there was an appreciable amount of blood-tinged joint fluid in the subacromial bursa. Curiously, in one man (Case 2) who had a one and one-half inch tear and was operated upon six days after injury, there was very little fluid in the bursa and this was not blood tinged. In the case which was not operated upon for 70 days, there was also little fluid in the bursa.

The size of the rupture in the tendons varied from slightly under one inch to two and one-half inches in length. In the case with the largest tear (Case 4), the rent apparently extended into the infraspinatus portion of the capsule (Fig. 5).

We did not find the biceps tendon grossly damaged in any case.

Diagnosis.—In the diagnosis of complete rupture Codman[6] has listed 18 conditions which should be present. We were able to examine one patient within six hours of the injury and another within 24 hours. In both of these all of Codman's conditions were fulfilled, *i.e.,* Occupation—labor. Age—over 40. No symptoms in shoulder prior to accident. Adequate injury—usually a fall. Immediate sharp, brief pain. Severe pain the following night. Loss of power of elevation of the arm. Negative roentgenogram. Little, if any, restriction when stooping. Faulty scapulohumeral rhythm, a tender point, a sulcus and an eminence at the insertion of the supraspinatus, which causes a jog, a wince and soft crepitus, as the tuberosity disappears under the

acromium when the arm is elevated, and usually also, as it reappears during descent of the arm.

In our cases pain was the most variable symptom. Three patients had sharp pain at the time of rupture and severe pain within 24 hours following the accident. One (Case 2) complained of only a dull pain in the shoulder which persisted, so that the following day he consulted a physician. Another (Case 5) said he had only slight pain immediately after his fall. He therefore paid no attention to it and did not consult a physician for 17 days. At that time his only complaint was inability to abduct his arm. He refused to submit to operation for 70 days. During this time the pain increased and it was for this reason he finally consented to operation.

Treatment.—One has but to see a complete rupture of the supraspinatus tendon to realize that there is only one form of treatment: Namely, to suture the tendon and to accomplish this without delay. Unfortunately, obstacles often prevent immediate surgical intervention. Our greatest difficulty was to obtain the consent of the patient. In one case it was necessary to convince the family physician of the existence of the lesion before he would advise operation.

The repair was comparatively easy in those cases operated upon within 13 days. The exploratory incision, described by Codman and by Wilson, was used in the four early cases, and a satisfactory repair was easily accomplished. The tendon was sutured, by means of drill holes, to the greater tuberosity, and the ends of the tendon were sutured together. Silk sutures were used.

In the case operated upon 70 days after rupture we found it necessary to use the saber-cut incision and the operation described by Wilson. However, silk was used instead of fascia lata.

Postoperative Treatment.—Postoperatively all patients were confined in bed with the arm placed in a position of abduction and external rotation, for at least five days. In Case 1 the arm was placed in an aeroplane splint at the end of this period. This was worn for 15 days before active motion was allowed. At present, approximately ten months after operation, he lacks 45 degrees complete elevation but is able to perform his regular work, to which he returned about four months after operation.

Case 3, which had the smallest tear we encountered, was operated upon 13 days after injury, and was kept in bed two and one-half weeks with the arm placed in a position of abduction and external rotation, before active motion was allowed. Four and one-half months later he lacked only 35 degrees of elevation. He returned to his regular work in a little over three months.

Another patient (Case 2), operated upon six days after rupture, was placed in bed with the arm in extreme elevation. A week later a plaster spica was applied to the shoulder which retained the arm in extreme elevation. The plaster encasement was worn for 18 days. Three months after opera-

tion he lacked only a few degrees of full elevation of the arm and was able to return to work.

In the case of the patient who was operated upon 70 days after injury, the arm was placed in an aeroplane splint following operation and left there for three weeks. Six months later he was only able to abduct the arm 85 degrees and still complained of some pain. He returned to his regular work five and one-half months after operation.

The only complication was in the oldest patient (Case 4), who had the largest tear and upon whom we operated six days after injury. In this case active motion was allowed within a week after the operation. In two weeks he was encouraged to actively exercise the arm. His range of abduction increased very slowly. Two months later he could abduct his arm to only 55 degrees, in the coronal plane. At that time roentgenograms showed a small shadow apparently in the subacromial bursa. A month and a half later there was an increase in the density of this shadow (Fig. 6). He could only abduct his arm 60 degrees.

We reoperated upon him five months after the original operation, and found a crescent shaped piece of bone on the floor of the subacromial bursa, with the points of the crescent pointing toward the tuberosity (Fig. 7). This mass was excised, and on inspection of the area of rupture, it was found to be firmly healed.

To have had this bone produced, some fragment of periosteum or osteogenic tissue must have been torn away from the tuberosity. This, coupled with hemorrhage, formed an ossifiable medium.[9] The subacromial bursa must also have been injured. We are of the opinion that following the trauma of both rupture and operation, too early motion produced the required amount of hemorrhage and injury to the bursa, to form the ossifiable medium.

With the exception of the patient who developed a complication, the poorest end-result was in the case of the man operated upon following a delay of 70 days. Not only was the operation more difficult but now the patient has the least range of motion of any of our cases and he still continues to complain of pain.

CASE REPORTS

Case 1.—C. S., a milkman, age 52, of medium height and good muscular development, fell on sidewalk February 7, 1936, landing on his right arm and right shoulder. Immediately following the fall he had a sharp pain in his right shoulder and was unable to abduct his right arm. He was examined six hours later. There was no swelling of the right shoulder or arm. He could abduct the right arm to only 45 degrees (Fig. 1). When it was passively abducted to 90 degrees he could then actively abduct it 45 degrees more. There was little restriction of motion when stooping. There was marked disturbance of the scapulohumeral rhythm. There was a very tender area over the greater tuberosity of the humerus. No definite sulcus was felt. There was a jog when the arm was abducted to about 60 degrees. The jog disappeared during descent of the arm. He complained of severe pain when the arm was externally rotated. A roentgenogram showed no bony abnormalities about the shoulder joint.

He was operated upon at the Hospital for Ruptured and Crippled, February 12, 1936. A three inch incision was made, extending downward from the acromioclavicular joint, and splitting the fibers of the deltoid. There was a considerable quantity of blood tinged fluid in the subacromial bursa. The articular surface of the humerus could be seen through a one and one-half inch tear in the supraspinatus tendon. The proximal portion of the tendon had retracted beneath the acromium. There was a ragged stub of tendinous tissue attached to the tuberosity of the humerus.

Four holes were drilled through the tuberosity of the humerus. The proximal end of the tendon was then pulled down and two mattress sutures of silk anchored it to the tuberosity. The margins of the rupture were then sutured together.

Following operation, the patient was placed in bed with his arm abducted to 90 degrees and in a position of external rotation. Seven days later he was allowed out of bed, with his arm held in a position of abduction by means of an aeroplane splint.

FIG. 1.—(Case 1.) Range of abduction before operation.

FIG. 2.—(Case 1.) Range of abduction nine months following operation.

This splint was worn for 15 days. After this time he was allowed active use of the arm.

On April 15, 1936, he could abduct his arm to 90 degrees in the coronal plane. There was still faulty scapulohumeral rhythm. Two months later he could abduct his arm to about 105 degrees. He returned to his regular work at this time. Nine months after the operation he could abduct his arm to about 115 degrees (Fig. 2). A month later there was a further increase of ten degrees in the range of abduction. He complained of only occasional pain in the shoulder and he had no difficulty in performing his regular work.

Case 2.—C. S., age 54, a milkman, slightly underweight but with good muscular development. He had a previous history of an injury to his left shoulder following a fall in 1933. On August 29, 1936, while delivering milk, he fell down four steps, falling on his flexed right elbow and on his back. Following the fall he was unable to abduct his right arm. He continued with his work, however. That night the pain became more severe. The following day he was unable to work. He was examined by us September 1, 1936.

There were no objective signs of injury of the right shoulder. He was unable to abduct his right arm beyond 50 degrees in the coronal plane. When the arm was passively abducted to a right angle, he could actively continue abduction about 20 degrees

further. There was little restriction of motion when stooping. There was faulty scapulo-humeral rhythm and a jog was present on both abduction and adduction. There was tenderness over the greater tuberosity of the humerus, most marked when the arm was placed in a position of dorsal flexion. A sulcus could be felt in the area of the insertion of the supraspinatus tendon. Both internal and external rotation of the arm caused pain. A roentgenogram showed no bony abnormalities around the shoulder joint.

He was operated upon at the Hospital for Ruptured and Crippled, September 4, 1936. The same type of incision was made as in Case 1. There was very little fluid in

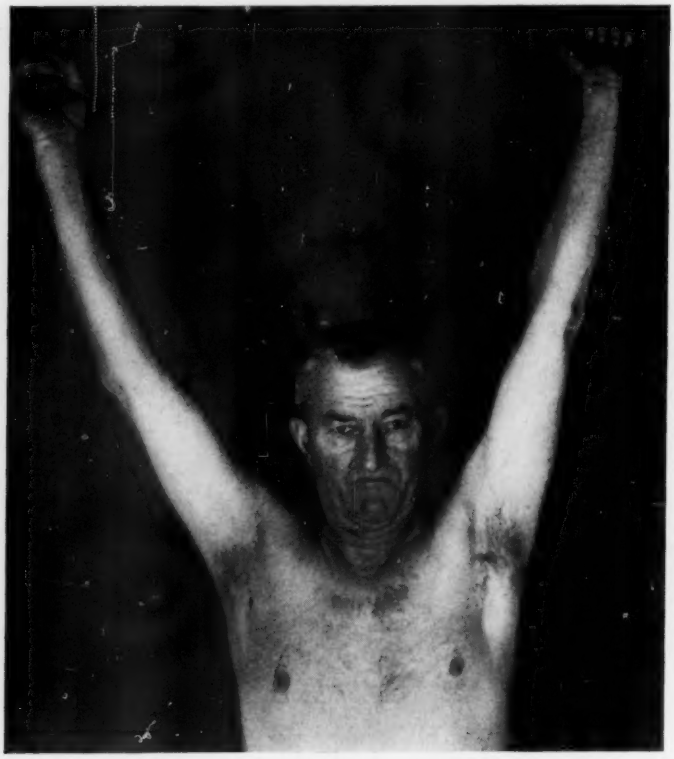

FIG. 3.—(Case 2.) Range of motion two months following operation.

the subacromial bursa. There was a one and one-half inch tear of the supraspinatus tendon, immediately proximal to its insertion, with a stub of irregular tendon attached to the tuberosity of the humerus. The proximal portion had retracted about one inch. It pulled down with ease and was repaired in the same manner as in Case 1.

Following the operation, the patient was placed in bed with the arm held in extreme elevation by tying it to the head of the bed. Six days later a plaster spica was applied to the shoulder holding the arm in the same position. The encasement remained on for 18 days. He was then allowed to use the arm.

Two months later (Fig. 3) the range of motion of the right arm was almost the same as that of the left one. He was able to return to his regular work December 8, 1936, at that time he lacked only a few degrees of complete elevation.

Case 3.—W. F., age 54, a milkman, of good muscular development. On June 23, 1936, as he was loading a case of milk bottles onto a truck, he felt a sharp pain in his left shoulder. Immediately following this he found that he could not abduct his left arm. He continued with his work, using his left arm as little as possible. That night

the pain became more severe and persisted. In spite of the pain he worked the following day, but the next day, June 25, 1936, he remained at home. Two days later his physician advised him to rest the arm, and told him that he had a "sprain of the shoulder." The pain continued. He was examined June 29, 1936.

On examination, there was no swelling of the left shoulder. He was unable to abduct his left arm beyond 30 degrees. The arm could be passively abducted throughout the whole range but he was unable to perform it himself. There was no restriction of motion when stooping. External and internal rotation caused pain. There was marked disturbance of the normal scapulohumeral rhythm. There was tenderness over the greater tuberosity of the humerus. No sulcus or eminence could be palpated. A roentgenogram showed no injuries of the bones of the shoulder joint.

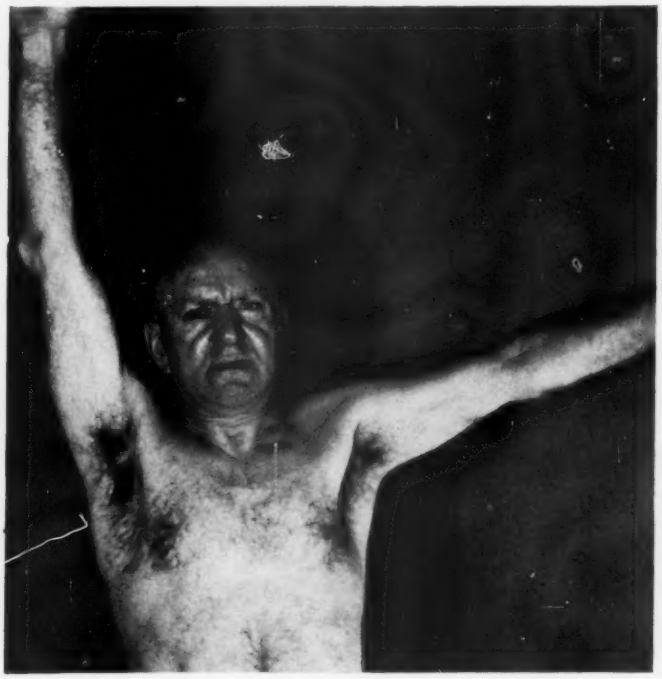

FIG. 4.—(Case 3.) Range of abduction three months following operation.

He was operated upon at the Hospital for the Ruptured and Crippled, July 6, 1936. The same type of incision was made as in Cases 1 and 2. There was a large quantity of blood tinged fluid in the subacromial bursa. There was a small tear of the supraspinatus tendon immediately proximal to its insertion. The tear measured slightly less than one inch. There was very little retraction of the proximal portion of the tendon. This was pulled down and sutured to the stub end of the tendon that was attached to the tuberosity.

Following the operation he was placed in bed with the left arm placed in a position of abduction and external rotation. He remained in bed with his arm in this position, for two and one-half weeks.

Two months after the operation he could abduct his arm to about 100 degrees. A month later he could abduct it about 25 degrees further (Fig. 4). He returned to his regular work October 10, 1936. On November 20, 1936, he had about 35 degrees less abduction of the left shoulder than of the opposite one. There was no complaint of pain when the arm was rotated.

Case 4.—G. H., age 58, a man of fair muscular development whose occupation was loading milk trucks. On June 2, 1936, while stacking boxes of empty milk bottles, a box, weighing about 20 pounds, fell and struck his left shoulder. He had sharp pain in the shoulder immediately, and he was unable to abduct his left arm. The pain was so severe that he stopped working. He was examined the following day.

On examination there was slight swelling over the left shoulder. He could abduct his left arm to 40 degrees in the coronal plane. There was slightly more abduction present in the sagittal plane. Following passive abduction of the arm to a right angle he could actively abduct it a few degrees further. However, active abduction from above 90 degrees produced pain and he was able to hold it in this position for only a few seconds. There was slight restriction of motion when stooping. There was marked

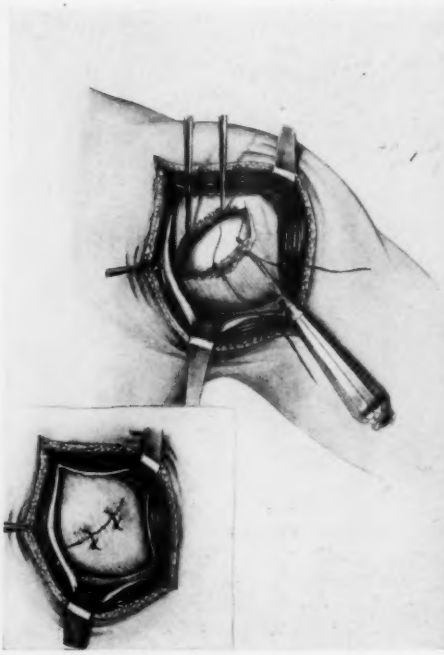

FIG. 5.—(Case 4.) A two-inch tear of the supraspinatus tendon as it appeared at operation. A drill is shown passing through the tuberosity.

FIG. 6.—(Case 4.) Roentgenogram showing bony mass in the floor of the subacromial bursa.

disturbance of the normal scapulohumeral rhythm. Both internal and external rotation caused severe pain. There was tenderness over the whole top of the shoulder joint. There was a jog present. A definite sulcus could be felt near the site of the insertion of the supraspinatus. A roentgenogram showed no fractures of the humerus or scapula.

He was operated upon at the Hospital for Ruptured and Crippled, June 8, 1936. An exploratory incision was made. There was a considerable quantity of blood tinged fluid in the subacromial bursa. A two and one-half inch tear was found in the supraspinatus tendon immediately proximal to its insertion (Fig. 5). The tendon had retracted about one inch. The rupture extended posteriorly into the infraspinatus portion of the capsule. The retracted portion of the tendon was sutured to the tuberosity in the same manner as in Cases 1 and 2.

Following the operation the arm was placed in a position of abduction and external rotation. The patient was allowed to move his arm as much as he wished. He was confined to bed for one week. He was then allowed to walk and he was encouraged to actively exercise his arm.

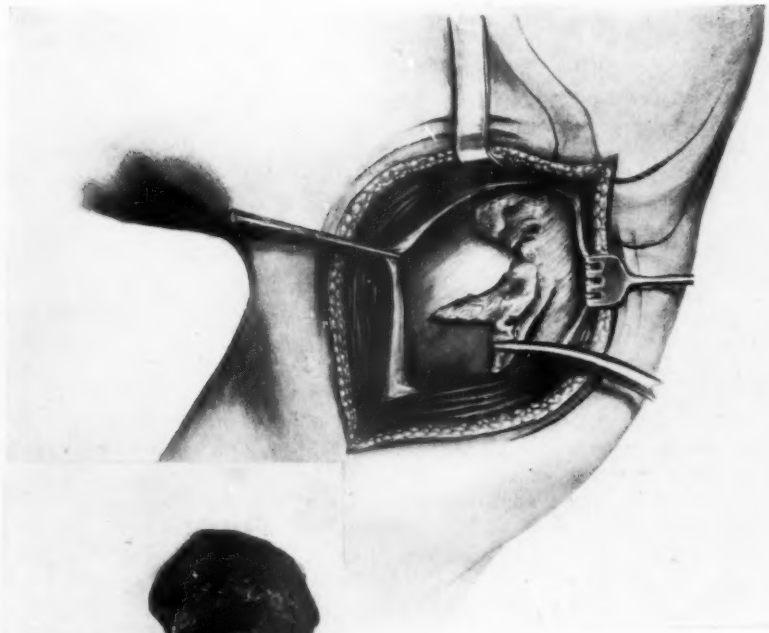

FIG. 7.—(Case 4.) Bony mass as it appeared during operation.

FIG. 8.—(Case 4.) Photograph of bony mass removed.

FIG. 9.—(Case 4.) Photomicrograph of section of bony mass.

On August 12, 1936, he could abduct his arm to only 55 degrees. A roentgenogram showed a small shadow apparently in the subacromial bursa. Diathermy treatments were started. On October 1, 1936, a roentgenogram showed an increase in the density of the shadow in the bursa. At this time he could abduct his arm to 60 degrees but it was painful. He was still receiving diathermy treatments. On October 29, 1936, a roentgenogram showed an increase in the size and density of the mass (Fig. 6).

On November 6, 1936, we reoperated upon the shoulder. Following splitting of the fibers of the deltoid we found no fluid in the subacromial bursa. There were adhesions of the bursa. Lying on the floor of the bursa was a crescent-shaped, hard mass with the points of the crescent pointing toward the tuberosity (Fig. 7). The body of this mass extended beneath the coraco-acromial ligament. The mass was excised (Fig. 8). It measured 4½ x 2 cm. Microscopic section showed bone trabeculae (Fig. 9). On inspection of the supraspinatus portion of the capsule, the area of rupture appeared firmly healed.

Case 5.—H. H., age 57, a milkman with well developed muscles. On January 1, 1936, he fell 12 steps landing on his left shoulder and left arm. He had slight pain in his shoulder following the fall, but paid little attention to it. Immediately after falling he found that he was unable to abduct his left arm. He continued working until January 17, 1936, when he was examined.

On examination, there was no swelling of the left shoulder. He could abduct his left arm to about 50 degrees. Following passive abduction of the arm to a right angle, he could actively abduct it about 20 degrees further. There was no restriction of motion when stooping. A jog was present. There was tenderness over the greater tuberosity of the humerus. A slight sulcus could be felt near the insertion of the supraspinatus tendon. A diagnosis of rupture of the supraspinatus tendon was made and he was advised to submit to operation. He refused and continued working.

He was reexamined February 28, 1936. At that time he complained of pain in his left shoulder, especially when he was working. There was atrophy of the spinati muscles. He could still abduct his arm to about 50 degrees. However, it could be passively abducted to only slightly beyond a right angle.

He was operated upon at the Hospital for Ruptured and Crippled, March 10, 1936. An exploratory incision was made and the fibers of the deltoid split. There was little fluid in the subacromial bursa. There was a two-inch tear in the supraspinatus tendon at its insertion. There was very little tendinous tissue left attached to the tuberosity of the humerus. The proximal portion of the tendon had retracted beneath the coraco-acromial ligament and could not be pulled down. The incision was then enlarged, the acromioclavicular articulation divided, and the base of the acromium was cut. This procedure exposed the proximal portion of the tendon. The tendon was brought down to the tuberosity and sutured to it with silk, by means of drill holes.

Following the operation the patient was placed in bed with his left arm in a position of abduction and external rotation. Five days later the arm was placed in an aeroplane splint and retained there for three weeks. Then active motion was allowed.

His range of abduction increased slowly and he complained of considerable pain. He was unable to return to work until near the end of August, 1936. At that time he could abduct his arm to only 85 degrees.

SUMMARY.—(1) We have operated upon five cases of complete rupture of the supraspinatus tendon during the past year.

(2) Our patients were all in the sixth decade of life.

(3) The immediate trauma causing this condition was a fall in three cases, a blow in one, and due to lifting in another.

(4) Pain was a variable symptom.

(5) The diagnosis soon after injury was not difficult.

(6) There was little retraction of the tendon in the four cases operated upon within 13 days following injury. There was considerable retraction where the time was longer.

(7) We had but one complication, a postoperative development of bone on the floor of the subacromial bursa.

CONCLUSIONS

Immediate repair is advised as the operation is easier and the end-result better than when it is delayed.

We believe that immobilization in elevation for from two to three weeks after operation is the most satisfactory after-treatment.

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PLASMA EXUDATION

LOSS OF PLASMA-LIKE FLUID IN VARIOUS CONDITIONS RESEMBLING SURGICAL SHOCK

AN EXPERIMENTAL STUDY

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Loss of whole blood has long been recognized as a factor in the production of secondary surgical and traumatic shock. The early shock that develops immediately after an injury before blood loss has had a chance to take place is sometimes considered to be psychic or neurogenic in origin.[1] Experimental and clinical observations[2, 3] have both indicated the importance of blood loss in the shock that occurs later. This blood loss occurs most obviously in cases of external hemorrhage, but also results in instances of hemorrhage into body cavities, hollow organs and tissue spaces.[4]

More recently it has been realized that in many traumatic and thermal conditions the fluid that leaks out from the blood stream is more plasma than whole blood. The proportions of plasma and whole blood may differ in the different conditions in question while in some of them erythrocytes are almost completely absent from the exudate and it may be considered essentially blood plasma. Analyses of the exudates have shown them to be similar to blood plasma in chemical composition, as shown in Table I.

The amount of blood loss in normal animals which will produce death has been differently reported by various observers. Boyce, Lampert and McFetridge[5] found that dogs could be bled 4.56 per cent body weight without shock or death resulting. Roome, Keith and Phemister[6] showed that 4.51 per cent blood loss would produce death in dogs, and Johnson and Blalock[7] found a comparable figure to be 5.1 per cent. Elman and Cole[8] found that death followed a 2.7 per cent loss of blood from hemorrhage in normal cats. Other experiments have shown that in certain conditions of traumatic or surgical shock, blood loss approaches or exceeds these figures.

Evidence indicates that the loss of less plasma than whole blood can be tolerated in experimental animals before death results. This evidence is obtained from plasmapheresis experiments. These latter are always open to the objection that the reinjection of centrifuged cells after the removal of plasma may introduce other factors, to be reckoned with, than the plasma loss. The centrifuged cells even if not hemolyzed may accelerate the onset of death in an already weakened animal. Johnson and Blalock[7] found that under certain conditions dogs would die after an average loss of 2.6 per cent body weight loss of blood plasma and blood by plasmapheresis. Roome,

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Keith and Phemister[6] in somewhat similar experiments found a figure of 4.4 per cent. Harkins and Harmon[9] reported that an average of 4.0 per cent body weight of plasma was removed from dogs by plasmapheresis before death resulted.

In various conditions data have been reported to show that a plasma loss approaching these figures may occur. These reports have usually been made separately and embody plasma loss in ten conditions, including burns, freezing, bile peritonitis, tissue autolysis in vivo, acute pancreatitis, pneumonia and pulmonary edema, intestinal manipulation, portal and mesenteric obstruction, externally strangulated colostomy loops and release of a constrictor of an extremity.

In the belief that it would be well to assemble data on plasma loss in all these conditions under one head, this paper has been written. No attempt will be made to prove in each instance that the loss of plasma is the sole or even the chief factor in the resultant death. Toxic products or nervous reactions are always to be considered. Although their importance is difficult to demonstrate, their presence is practically impossible to disprove. Hence, the extent of plasma loss in the ten conditions will be simply listed in order. Two factors make the exudation of a certain amount of fluid in these conditions of much more serious import than the loss of a similar amount of usually more watery fluid in certain so-called internal medical conditions. The first of these is the rapidity of the loss. In all the surgical conditions discussed in this paper, the loss of plasma-like fluid is of rapid occurrence, taking place in only a few hours. The transudates in ascites, pleural effusion, edema of the extremities, *etc.*, are usually of a more chronic type and are slower of formation. The second factor is the protein content which is similar to blood plasma in the conditions discussed in this paper, but is low in the transudates occurring in ascites, pleural effusion, edema of the extremities, *etc.* To epitomize by an example, one can easily lose two liters of urine in a day, but would not advisedly part with two liters of blood in the same time.

Burns—Blood concentration has been noted in burns by several authors. Tappeiner,[10] in 1881, was the first to report this finding. One of his patients had a red count of 9,000,000 following a severe burn. Locke,[11] in 1902, reported four cases of burns with a red count of 9,000,000 or more. Underhill,[12] in 1923, reported hemoglobin percentages as high as 209. Blalock[13] found that in experimental burns the hemoglobin may rise to 130 per cent. Harkins[14, 15] found that in experimental burns the hemoglobin may reach 162 per cent and the hematocrit reading 72. He further showed that the blood concentration is proportionate to the extent of plasma leakage into the burned tissues, but that the blood pressure may remain compensated until near the end, only to collapse just before death. The extent of this fluid loss was measured by Underhill,[16] Blalock,[13] and by Harkins.[14, 15] The first author measured the amount of fluid expressed from the water-logged burned tissues; the second, by burning one lateral half of an anesthetized animal

and then after careful sagittal bisection, comparing the weight of the burned and unburned sides; and the third by burning one lateral half of an anesthetized animal placed on a balanced apparatus and measuring the amount of displacement caused by the increase in weight of the burned side. The total amount of loss of fluid was found to equal 3.2 per cent body weight (Blalock[13]) or 2.2 per cent (Harkins[14, 15]). In human beings there is the additional factor of leakage of fluid from the weeping burned surface. These three investigators showed that the fluid that escaped into the tissues was chemically similar to blood plasma. There was a decrease in the cardiac output and in the bleeding volume in shock following burns.[18, 19]

FREEZING.—The authors showed[20, 21, 22, 23, 24] that in freezing a portion of the body there was a leakage of fluid from the blood stream into the frozen or thawing tissues with a resultant blood concentration and lowered bleeding volume. Solid carbon dioxide was applied to about one-fourth of the body surface of ten completely anesthetized dogs and left in place for about an hour, at the end of which time the underlying tissues were thoroughly frozen. Frequent blood pressure readings, hemoglobin percentages and hematocrit readings were determined.

In a series of ten experiments, the initial blood pressure averaged 148 and the final blood pressure 81 Mm. of mercury. This amount of blood pressure lowering may be considered arbitrarily as within the limits of so-called surgical shock. After a period averaging 21 hours from the time of freezing, four of the dogs were dead and the other six were killed. Nine of the animals were then carefully bisected by the method previously described,[15] and a comparison made of the weights of the frozen and unfrozen sides. The average difference amounted to 2.55 per cent of the total body weight. Incision into the tissues that had been frozen revealed sufficient plasma-like fluid to account for the difference in weight. This amount of plasma, if lost from the blood stream, is sufficient to account for a large part of the shock present in these animals. In eight burn experiments previously reported,[15] the amount of fluid shift at death was 2.2 per cent of the total body weight.

The blood concentration changes began almost immediately after the freezing and were present long before the blood pressure had fallen markedly. It is seen from Table I that in all animals there was an increase in hemoglobin percentage and hematocrit reading. The average hemoglobin percentage before freezing was 96 and after freezing was 134. The average hematocrit reading before freezing was 47 and after freezing 66. The figures obtained in Experiment 10 are higher than in any readings obtained in shock due to burns, except by Underhill in human beings. Control experiments showed no marked blood concentration and no fluid shift.[15]

By making multiple incisions into the edematous tissues, sufficient fluid was drained out for chemical analysis. The average results of nine such analyses are given in Table I. The fluid was only slightly tinged with blood, but clotted if no anticoagulant was added. The sugar concentration was

TABLE I

A COMPARISON OF THE CONCENTRATION OF CERTAIN SUBSTANCES IN BLOOD PLASMA AND IN THE FLUID LOST FROM THE BLOOD STREAM IN VARIOUS CONDITIONS*

Fluid	Sugar	NaCl Mg. per 100 cc.	Nonprotein Nitrogen	Protein Gm. per 100 cc.
1. Burns[38]	134	686	62	7.6
2. Freezing[21]	67	697	50	3.6
3. Bile peritonitis[28]	60	516	32	4.3
4. Tissue autolysis in vivo[29]	83	565	71	7.6
5. Acute pancreatitis	no data	no data	no data	no data
6. Pneumonia and pulmonary edema[32]	no data	631	no data	no data
7. Intestinal manipulation[38]	221	616	61	6.2
8. Mesenteric obstruction[41]	215	577	36	3.0
9. Externally strangulated colostomy loops	137	689	21	4.5
10. Release of a constrictor of an extremity[43]	no data	619	47	4.4
Average	131	622	48	5.2

*Control values for blood plasma[21] were: Sugar, 104; NaCl, 676; nonprotein nitrogen 54 mg. per 100 cc.; protein 4.2 Gm. per 100 cc.

in general lower in the fluid than in the blood plasma. The chloride concentration was approximately the same in blood plasma and in the tissue fluid. The fluid usually contained slightly less nonprotein nitrogen and protein than blood plasma. In a series of five animals in which the blood pressure was reduced to a shock level by freezing before bleeding, the bleeding volume averaged 2.0 per cent body weight.

BILE PERITONITIS.—The idea has previously been advanced,[25] from data obtained by experiments on animals, that toxic action and anaerobic bacterial invasion are the two chief lethal factors in bile peritonitis. From other data similarly obtained by experiment, we have, in collaboration with Andrews and Hudson, advanced the idea that secondary shock (in the sense of decrease in volume of circulating fluid) is one of the most important lethal factors in this condition.[26, 27, 28] We fully recognize that there are substantial differences between experimental and human bile peritonitis. However, since the theories of the previous workers were obtained by experiment, refutation of these theories can come only from similar experiments. It is after this that application of the theories to patients can be made.

No attempt will be made at this time to present proof against the toxic or bacterial theories of death in bile peritonitis, but a brief outline will be given of the positive evidences for the rôle of secondary shock in this condition. The presence of secondary shock is significant because its therapeutic implications are clear.

Dogs under general anesthesia were used in all experiments. The per-

tonitis was produced by the intraperitoneal injection of 5 cc. per Kg. body weight of either 10 per cent bile salt solution or whole gallbladder bile. The animals were then observed until death, a matter of hours later.

The most striking result of the biliary action was a gradual but profound lowering of blood pressure with a markedly lowered bleeding volume. Accompanying this fall in blood pressure was a marked concentration of blood in all of 32 dogs observed, and in three instances the hemoglobin rose to the extreme values of 177, 178, and 190 per cent respectively. As the peritonitis developed there was an enormous effusion of blood stained fluid into the peritoneal cavity. This fluid was not a mere transudate, but clotted spontaneously and was shown to be chemically similar to blood plasma in total protein, sugar, sodium chloride, and nonprotein nitrogen content. For example, in one typical experiment the plasma protein was 6.3 Gm. per 100 cc. and the fluid protein 5.7 Gm. In 27 experiments the amount of this peritoneal fluid averaged 2.5 per cent body weight, which corresponds to 250 cc. in a 10 Kg. dog. Since an average of 0.4 per cent body weight of bile or bile salt solution was used in these experiments, and since not all of this may have been absorbed, a corrected value for the amount of peritoneal fluid would be 2.1 per cent body weight.

It is assumed that this outflow of plasma-like fluid accounts for a large part of the blood concentration with increased hemoglobin percentage, for the decreased bleeding volume, and for the marked fall in blood pressure. It may be difficult to visualize how this amount of plasma loss can be of such importance. The question as to whether it is enough to entirely explain the death of the animals under consideration is not within the province of this paper. But when it is remembered that this amount of fluid corresponds to a hemorrhage of two liters of blood in an average sized man, its significance becomes more manifest. Blalock[3, 13] and others have shown that a somewhat similar loss in burns, trauma to an extremity, intestinal manipulation, and other conditions is sufficient to cause death. The same evidence indicates its importance in the production of secondary shock and the resultant death in bile peritonitis.

Tissue Autolysis In Vivo.—While extensive loss of plasma-like fluid into the peritoneal cavity seems to be a lethal factor of importance in experimental bile peritonitis, the evidence that such is the case in death due to experimental implantation of liver in the peritoneal cavity is not only inconclusive but instead it seems to point toward other causes.[29] In experimental bile peritonitis gram-positive anaerobic bacilli were found in only a small proportion of cases and then usually as either late or postmortem invaders. In peritonitis following liver implanation on the other hand, such organisms were found in all instances. It is quite possible that these organisms act chiefly in breaking up the liver or other tissue into toxic substances. Such action may be chemical in producing toxic proteose-like substances or may be merely mechanical with disruption of the tissue into finer particles, due to the explosive action of the gas. When broken up into such particles the

action may be partly that of a local irritant producing some local fluid loss and partly that of a general toxic agent. In addition some of these substances may give rise to a generalized increased permeability of the vascular system with a generalized loss of circulating blood fluid. It is only by considering these factors working simultaneously that a complete picture of the mechanism of death due to liver implantation can be drawn. At the present time it seems unwise to say that one of these factors is the only element of importance or even the chief instrument of death. These causes may work coördinately in bile peritonitis as well, but in the latter the local irritating effect of the bile produces such a regional outpouring of fluid that the factor of secondary shock outweighs and overshadows the rest. In liver autolysis on the other hand, the less irritating broken-down liver juices may produce a general toxic action out of proportion to the local fluid loss before the latter has reached dangerous proportions.

While certain of these experiments, especially those on bile peritonitis, indicate that there is such a thing as irritative peritonitis in which local fluid loss may be a lethal factor of importance, the exact cause of death in all instances is not clear. The peritoneal cavity in liver autolysis experiments contains a vicious mixture of irritant, foreign body, bacteria and injured tissues of the host. To say that there is one cause of death in such a case is difficult.

TABLE II

BLEEDING VOLUME IN VARIOUS CONDITIONS IN WHICH PLASMA HEMORRHAGE OCCURS*

Condition	Bleeding Volume Per Cent Body Weight
1. Burns[19]	1.6
2. Freezing[23]	2.0
3. Bile peritonitis[28]	1.8
4. Tissue autolysis in vivo[29]	2.2
5. Acute pancreatitis	no data
6. Pneumonia and pulmonary edema	no data
7. Intestinal manipulation[6]	1.4
8. Mesenteric obstruction	no data
9. Externally strangulated colostomy loops	no data
10. Release of a constrictor of an extremity	no data
Average	1.8

*Control values for the bleeding volume of animals under barbital have been reported: 5.2,[44] 4.5,[6] and 4.17 per cent of body weight.[19] In primary types of shock the bleeding volume is usually above 3.0 per cent (*e.g.*, following histamine injections, 3.6 per cent), and in secondary types of shock is below 3.0 per cent (*e.g.*, following trauma to an extremity, 1.7 per cent).

In experiments where peritonitis was produced by the intraperitoneal insertion of fresh, of autoclaved, and of contaminated liver, there was an outpouring of peritoneal fluid which, on analysis, proved to be similar to blood plasma. The importance of these analyses is partially vitiated by the presence of degenerated tissue proteins from the implant, but the fact

that most of the samples clotted spontaneously indicates the presence of considerable blood protein. There was marked blood concentration in many of the experiments as shown in Table III and a decrease in bleeding volume as shown in Table II. The amount of peritoneal exudate in the first five experiments in which liver was used averaged 2.6 per cent body weight but under certain conditions was much less than this value.

TABLE III

BLOOD CONCENTRATION IN VARIOUS CONDITIONS IN WHICH PLASMA HEMORRHAGE OCCURS

Condition	Hemoglobin: Increase as Per Cent Increase over Control Reading	Hematocrit: Increase as Per Cent Increase over Control Reading
1. Burns[19]	27	28
2. Freezing[20]	40	40
3. Bile Peritonitis[28]	48	43
4. Tissue autolysis in vivo	37	42
5. Acute pancreatitis	no data	no data
6. Pneumonia and pulmonary edema	66	no data
7. Intestinal manipulation[38]	48	no data
8. Mesenteric obstruction[41]	57	no data
9. Externally strangulated colostomy loops	no change	no change
10. Release of a constrictor of an extremity	no data	no data
Average	46	38

ACUTE PANCREATITIS.—In nine of a series of 30 cases of acute pancreatitis, De Takats and Mackenzie[30] reported red counts of over 5,000,000. One patient had a count of 7,000,000, another of 8,300,000 (with 140 per cent hemoglobin) and the rest varied from 5,200,000 to 5,700,000. Edema with hemorrhagic exudate in the peritoneal cavity was noted in several cases and shock was often present. Moon[31] reported a case of acute pancreatitis in a woman with a red count of 6,400,000 and a hemoglobin percentage of 112. Since the edema that results in this condition is largely retroperitoneal, its exact quantitative measurement is difficult. The reports of "sterile serofibrinous peritonitis" indicate the high protein content of the peritoneal exudate.

PNEUMONIA AND PULMONARY EDEMA.—Underhill and his associates[32, 33, 34] performed experiments during the World War on the effects of chlorine, phosgene and chloropicrin gas. He showed that these lung irritants caused massive pulmonary edema with marked blood concentration. The total extent of this edema was not measured, but it was shown to be due to a protein containing exudate. The average increase in blood concentration of four dogs which inhaled 41 to 50 parts per million of phosgene for one-half hour was 166 per cent of the control value as measured by hemoglobin readings. Underhill[35] showed that in the influenzal pneumonia that occurred during the time of the War, a similar pulmonary edema with resultant blood concentration is one of the chief lethal factors. He showed that fluid introduction might be of aid in this condition and that by following blood concentration changes, prognostication is greatly aided. In 11 cases with no complications, nine had a hemoglobin percentage of over 120 with values

going up to 140. Moon[31, 36] also noted red counts of 6,000,000 to 8,000,000 with correspondingly high hemoglobin percentage in influenzal pneumonia. He noted at autopsy of these patients that there was extreme capillary congestion of the mucosa of the pulmonary and gastro-intestinal tracts, that the lungs were wet and bloody and that frequently there was an effusion of reddish fluid in the serous cavities. Moon and Morgan[37] produced pulmonary edema in dogs by injections of sodium glycocholate with increase in the red count and hemoglobin percentage (2,300,000 and 35 per cent increase, respectively, in one dog). All of these results indicate that pulmonary edema may result from both exogenous and endogenous toxic factors.

Intestinal Manipulation.—Beard and Blalock[38] showed that intestinal manipulation in dogs produces an extensive weeping of the visceral peritoneal surfaces that is an important causative factor in the resultant shock-like syndrome. It is of interest to note that the results of Swingle and Parkins[39] are not entirely in agreement with those of Beard and Blalock. Swingle and Parkins found that even two and one-half hours of vigorous intestinal stripping had little effect on the blood pressure. Beard and Blalock[38] found a reduction in blood pressure to a shock level after intestinal manipulation with blood concentration and outpouring of fluid that was similar to blood plasma in chemical composition. Johnson and Blalock[40] showed that accompanying the reduction in blood pressure there was a marked lowering of the cardiac output, and Roome, Keith and Phemister[6] reported a lowered bleeding volume as shown in Table II. None of these authors reported a measurement of the total quantity of fluid lost, as indeed this would be difficult to do because of the large amount of fluid that accumulates in the intestinal walls, lumen and mesentery.

Portal and Mesenteric Obstruction.—The literature on fluid loss in experimental obstructions of this type has been reviewed in extenso by Harkins.[41] This writer presents clinical cases in which a measurement of the fluid loss is noted. Some of the cases showed a marked blood concentration. Distention is often observed and free fluid should be searched for. Vomiting and melena are sometimes present and the signs of intestinal obstruction are a feature, except that auscultation of the abdomen frequently reveals a preternatural lack of sounds. At operation or necropsy the infarction is usually hemorrhagic even in the arterial type, due to inflow of blood from the collateral vessels as shown by Mall and Welch.[42] The intestinal loop contains less gas and more fluid than most other types of obstruction, the bowel and mesentery are boggy and edematous, and there is considerable free fluid in the abdominal cavity. This fluid is apt to be more abundant in venous occlusion, while perforation of the intestine is more apt to follow arterial obstruction. The amount of local blood loss into the infarcted organs and into the peritoneal cavity has been shown experimentally to be sufficient to account for death of the animals in question. Few observations have been made concerning quantitative estimations of this fluid loss in clinical cases. Some observers, such as Moon,[31] have realized that shock may be

a factor in death in this condition. In certain cases it is quite certain that the fluid loss is not sufficient to account for death. Secondary peritonitis and the intestinal obstruction itself are lethal factors of importance here as they are in other conditions.

Externally Strangulated Colostomy Loops.—Under certain conditions the writers have seen colostomy loops that became constricted at the outlet from the abdominal wall with resultant swelling and exudation of plasma-like fluid. That this condition is probably associated with primarily venous blockage is indicated by the fact that in cases where the ends of one barreled loops become completely necrotic, no such exudation occurred. In three cases a rather marked leakage of fluid occurred as follows: In one of these the patient seemed to be in impending shock and when a blood transfusion was given and the loop was removed, preventing further plasma loss, she was much improved.

CASE REPORTS

Case 1.—E. L., housewife, age 27. Operation of exteriorization of the cecum, terminal two feet of the ileum and a portion of the ascending colon for terminal ileitis. The mesentery was divided, its blood vessels were tied off and the abdomen closed around the exteriorized bowel with catgut and silk. No rubber tube was used and no sutures were used to fasten the bowel to the skin. The blood pressure at the close of the operation was 120/80 and the patient was given 1,500 cc. Ringer's solution subcutaneously at 12 hour intervals. The day after operation the large dressings were soaked three times with an enormous amount of serosanguinous material. This material was not measured or analyzed and no blood concentration studies were made. Thirty-six hours after the operation the blood pressure had fallen to 100/70, the pulse had risen to 160 and the patient seemed much worse. The loop, which was edematous but not gangrenous, was clamped off and a 600 cc. blood transfusion given with resultant improvement, the blood pressure rising to 118/98 an hour later.

Case 2.—Mrs. M. S., artist, had a midline celiotomy for carcinoma of the rectosigmoid. A loop of the transverse colon was brought out through a separate incision in the epigastrium without ligating the mesenteric vessels or suturing the bowel to the skin or using a tube beneath the bowel. Sixty hours after the operation the bowel had prolapsed so that 12 cm. of it were outside and leaking considerable plasma-like fluid. The rate of formation of this fluid was measured as 60 cc. per hour. Analysis of the fluid, as shown in Table I, indicated its similarity to blood plasma. There were no appreciable blood pressure, pulse or temperature changes, and no blood concentration studies were made. The loop was decompressed by inserting a catheter with resultant marked decrease in the plasma leakage before the leakage had continued for more than three or four hours. The case is cited to show that, when watched for, a considerable amount of fluid may be found coming from the exteriorized bowel.

Case 3.—S. S., retired storekeeper, age 71, had a left rectus hypogastric incision for carcinoma two inches proximal to the terminal sigmoid. The peritoneum was incised on either side for a distance of four inches downward on the rectum and above on the sigmoid, and the terminal mesosigmoid was divided and ligated off. The superior hemorrhoidal artery was clamped and divided in order to bring the bowel upward and forward. The raw surfaces were closed with catgut and the loop of sigmoid was brought out. The edges of the mesosigmoid were sutured to the peritoneum and the muscle aponeurosis at the lower end of the wound. The upper end of the wound was closed with catgut and silk. During the ensuing 48 hours the exteriorized loop leaked so much plasma-like fluid that it was clamped off and removed. Beginning on the evening

of the operation the dressings became repeatedly saturated with a serosanguinous fluid that left them stiffened when they dried. Some of the fluid was analyzed and found to be chemically similar to blood plasma in nonprotein nitrogen, chloride, sugar, and protein content. In one 24 hour period 400 cc. of such plasma-like fluid were squeezed from the dressings. Blood studies revealed a slight hemoglobin concentration (114 per cent) but the hematocrit reading and red count remained normal. No blood pressure studies were made, but the pulse and temperature remained normal.

With the possible exception of the first of these three cases, the extent of fluid leakage was not of serious import. Chemical analysis in two instances revealed the plasma-like nature of the fluid and indicated the possibility of serious effects in cases where a larger amount of bowel might be exuded. The rate of formation of the fluid (60 cc. per hour) is considerably less than that lost in fatal cases of experimental bile peritonitis (350 cc. per hour calculated in proportion for man) as shown by Harkins.[28]

Release of a Constrictor of an Extremity.—Aside from the evident danger to the nutrition of the local part of keeping a tourniquet on too long, there is the occasional circulatory depression which has been observed in man following the release of the constricting agent. There is usually a sharp primary fall in blood pressure with rapid recovery to nearly the previous level and a more gradual secondary fall over a period of hours. Wilson and Roome[43] constricted one hind limb of dogs for from two to 20 hours. About two-thirds of the animals died at intervals of from five to 52 hours after release of the constrictor. There was in no case noticeable swelling of the limb during the period of constriction. In all cases a marked swelling of the limb gradually developed during the hours following the release of the constrictor. At necropsy the constricted legs were grossly swollen, boggy and discolored, and analysis of the contained fluid showed it to be similar to blood plasma, as shown in Table I. Comparison of the weight of the hind quarter sections of these animals showed an excess in weight of 3.54 per cent body weight. Survival of the animal after prolonged constriction of a limb was obtained by amputation of the limb followed by transfusion of blood, but not by transfusion alone as the limb only swelled the more or by amputation alone. Wilson and Roome[43] concluded that the fall in blood pressure and death are probably due chiefly to the withdrawal of water and plasma proteins from the general circulation to produce local swelling of the constricted limb.

Comment.—There are traumatic conditions of a nature in which the blood vessels are injured to an extent that only, or chiefly, plasma rather than whole blood leaks out. Mechanical injuries in which vessels are cut or ruptured usually lead to whole blood loss. The ten conditions discussed in which plasma loss occurs represent a somewhat different type of trauma in which the injury involves especially the capillaries. (1) Burns and freezing represent thermal trauma, while (2) bile peritonitis, tissue autolysis in vivo and acute pancreatitis may represent chemical trauma. In pneumonia and pulmonary edema the capillary injury may be either chemical or toxic.

(3) Intestinal manipulation is a form of mechanical trauma, but depends on a continued mild trauma over a prolonged period rather than a sudden rapid gross trauma. (4) In portal and mesenteric obstruction, externally strangulated colostomy loops, and release of a constrictor of an extremity, the chief factor seems to be capillary damage due to inadequate circulation. It thus seems that trauma of a thermal or chemical nature, mild continued mechanical type, or due to inadequate circulation is the sort of trauma especially likely to lead to exudation of plasma-like fluid from the blood stream. In many instances this fluid is lost in quantities sufficient to be of serious import, as shown in Table IV. No attempt is made to state the extent to which this

TABLE IV

TOTAL PLASMA-LIKE FLUID RECOVERED IN VARIOUS FATAL CONDITIONS EXPRESSED AS PERCENTAGE OF BODY WEIGHT*

Condition	Loss of Plasma-Like Fluid in Per Cent Body Weight
1. Burns	3.2,[13] 2.2[15]
2. Freezing[20]	2.6
3. Bile peritonitis[28]	2.5
4. Liver autolysis peritonitis[29]	2.6
5. Acute pancreatitis	no data
6. Pneumonia and pulmonary edema	no data
7. Intestinal manipulation	no data
8. Mesenteric obstruction[8]	5.2
9. Externally strangulated colostomy loops	no data
10. Release of a constrictor of an extremity	3.5
Average	3.1

* Control values in death following plasmapheresis have been reported as 2.6 per cent body weight (Johnson and Blalock[7]), 4.0 per cent (Harkins and Harmon[9]) and 4.4 per cent Roome, Keith, and Phemister[6]).

fluid loss operates in the causation of morbidity or death. Suffice it to say that in a variety of conditions there is a loss of plasma-like fluid from the blood stream in amounts approaching fatal plasma losses in plasmapheresis experiments. The fact that usually the plasma loss in the shock-like conditions is a little less in all instances than in shock due to plasmapheresis is suggestive of additional factors. In these various conditions the relative importance of plasma loss as a lethal factor varies considerably. As an example, loss of plasma-like fluid seems to be much greater in fatal experimental bile peritonitis than in the closely related peritonitis due to intraperitoneal implantation of autoclaved liver.

SUMMARY AND CONCLUSIONS

(1) Plasma-like fluid is lost from the blood stream in a variety of conditions. These include burns, freezing, bile peritonitis, tissue autolysis in vivo, acute pancreatitis, pneumonia and pulmonary edema, intestinal manipu-

lation, portal and mesenteric obstruction, externally strangulated colostomy loops, and release of a constrictor of an extremity.

(2) The types of trauma which produce these conditions can be roughly divided into (1) thermal trauma, (2) chemical and bacterial trauma, (3) mild continued mechanical trauma, and (4) capillary injury due to inadequate circulation.

(3) The amount of plasma-like fluid lost in these conditions approaches that which, when removed experimentally in plasmapheresis experiments, will produce death. Even in cases where the amount of fluid lost is not sufficient to cause death, it is often of sufficient importance to be recognized.

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WOUND HEALING AND NEOPLASIA *

AN EXPERIMENTAL INVESTIGATION

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THE development of epidermoid carcinoma at the site of chronic ulceration in the skin and mucous membranes, and at the sites of chronic irritation, not always accompanied by ulceration, has led to the assumption that the reparative stimuli constantly acting upon the cells in these regions sometimes lead to malignant degeneration.

It was believed that the carcinogenic activity of tar is due to its "irritative" properties. Accordingly, a number of observations have been made to observe whether "irritation" would reinforce the carcinogenic property of tar. The results have been conflicting. Deelman,[1] Teutschlaender[2] and Reding[3] reported that the latent period in the production of tar cancer was shortened by repeated scarification of the tarred areas in mice. Raposo,[4] Babes and Serbanesco[5] observed a similar influence of scarification on the development of epitheliomata in tarred rabbit's ears. Truffi[6] reported that in mice trauma accelerated the appearance of benign papillomata but did not hasten malignant degeneration. Choldin[7] applied test tubes containing hot water at 65° to 85° C. at repeated intervals to the tarred areas in mice and noted that carcinomata developed in about half the time required in controls.

On the other hand, Roussy, Leroux and Peyre,[8] and Ludford[9] could obtain no evidence that repeated scarification hastened the development of tar cancer. Daels[10] could not observe an increase in the carcinogenic activity of tar as a result of implantation of tar soaked threads or strips of tarred skin and the biweekly application of a "dull" cautery. Parodi[11] found that preliminary burning did not favor the subsequent development of tar cancer. Derom[12] observed that the repeated application of lead shields heated to 60° to 70° C. led to thickening of the skin and that these areas appeared more resistant to the carcinogenic action of tar than normal skin.

Since the epochal work of Kennaway, Hieger, Mayneord, Cook, and their co-workers on the identification and synthesis of carcinogenic hydrocarbons, it would appear that tarring as a method of experimental cancer production is obsolete because tar is a highly complex substance of varying composition. Berenblum[13] applied 1:2:5:6 dibenzanthracene, a carcinogenic hydrocarbon, to the backs of mice twice a week. In addition one-half of the animals received applications of .05 per cent solution of mustard gas in liquid paraffin, this being a potent chemical irritant. Among ten sur-

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vivors of the control group, nine had developed tumors by the fortieth week, whereas in the eight survivors of those that had received mustard gas, none showed even a benign papilloma by this time. As far as the writers have been able to determine, no other reports have as yet been published on studies of the relationship of wound healing and the action of the carcinogenic hydrocarbons.

The purpose of the following experiments was to observe if cutaneous epithelium, proliferating as a result of the "wound healing" stimulus, was more susceptible to the action of a potent carcinogenic compound than cutaneous epithelium in the normal static state.

The test animals were white mice of varying age, but at least six months old, procured from a commercial dealer and therefore of unknown genetic history.

The carcinogenic substance employed was 1:2 benzpyrene purchased from the Union Chimique Belge, Bruxelles. It was applied as a 1 per cent benzene solution, one to two drops three times a week, to the interscapular region of the back. The solution rapidly spread to the occipital region, to the lower back and upper lateral aspects of the trunk.

Thirty animals were employed as controls but only 17 survived for a sufficient period of time to be utilized in the experiment. Five of the animals not included in the results did not develop skin tumors although they lived throughout the period of chemical application.

In 50 animals large wounds were produced on the back at the level of the scapulae. Nineteen animals survived for sufficient periods to be tabulated. Of the 31 animals not considered six did not develop skin tumors, and the others died after varying periods shortly following the applications.

The latent period before papillomata first appeared was 50 to 65 days among the controls with one lesion developing in 40 days. No distinction is made between benign and malignant growths because with only one exception (BXNE) carcinomata eventually developed in all cases (but not, of course, from all benign lesions). The papillomatous growths arose at various sites on the back, some in the central portions of the exposed area and others at the periphery.

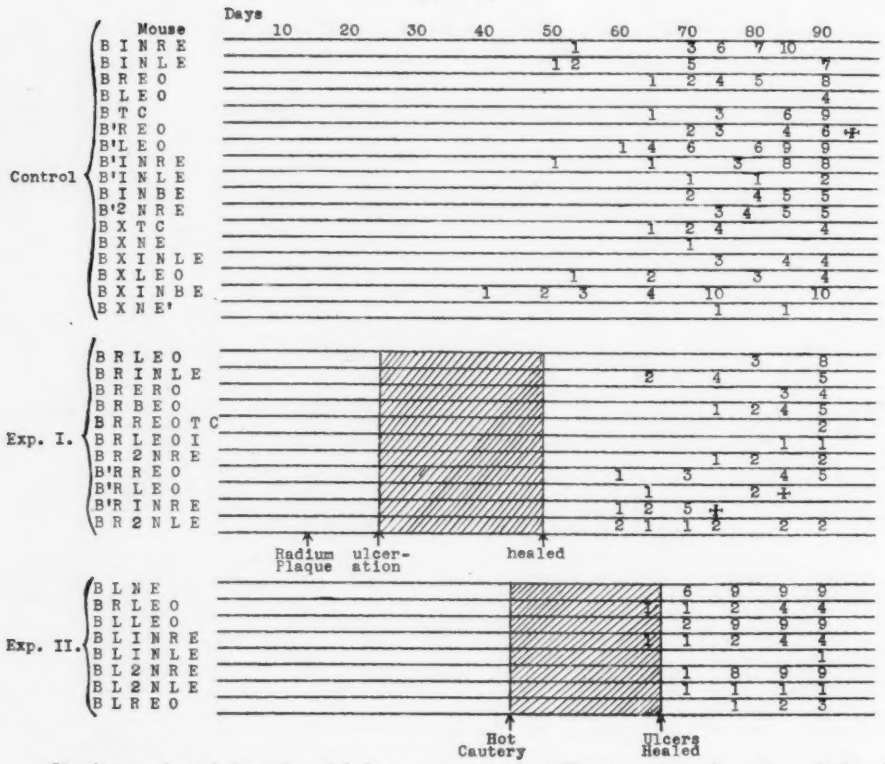
EXPERIMENTAL PROCEDURES

Experiment I.—After application of 1:2 benzpyrene three times a week for two weeks a "full strength" radium plaque was applied for 20 minutes to the interscapular region. The plaque contained 10 mg. of radium salt spread over 1 sq. cm., and the filtration was a thin layer of brass. By the end of ten days ulcerations began, these finally became a little less than 1 sq. cm. in size in all cases. The rate of healing was quite uniform and occurred with cicatrization, and some contraction of the wound about 25 days after the ulcerations began.

The triweekly applications of benzpyrene were not interrupted. The material was dropped upon the skin at the point of application of the radium after this occurred and upon the ulceration when this developed. The papillomata which subsequently appeared developed at points *about* the sites of ulceration and only in one instance did a papilloma occur in the skin recently formed over the ulcer. In this case, however, multiple papillomata also developed in the surrounding areas. As the latter grew some of them extended into the healed surfaces.

Experiment II.—A procedure similar to the one described above was carried out except that a metallic cautery heated to red heat was applied 45 days after the beginning of the benzpyrene application, producing an area of third degree burn of the skin approximately 1 x 1 cm. Following this the benzpyrene was dropped upon the burn, but spread over adjacent areas of skin also. By the end of the twenty-second day (±2 days) after cauterization all ulcers had healed. In two cases papillomata

TABLE I



Showing number of days elapsed before appearance of papillomata and carcinomata on backs of mice painted with 1 per cent benzene solution of benzpyrene. The increasing figures in right portion of table indicate increasing number of skin lesions.

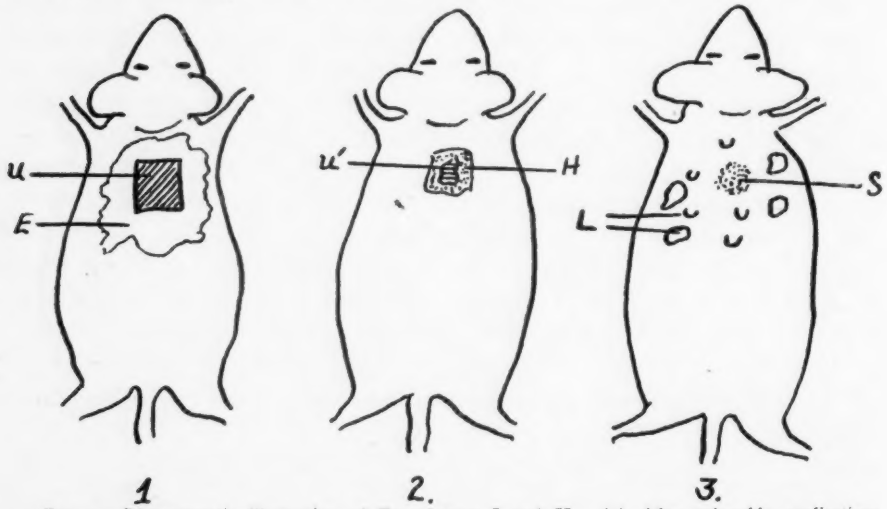


FIG. 1.—Diagrammatic illustration of Experiments I and II. (1) After triweekly applications of 1 per cent benzene solution of 1:2 benzpyrene to back of mouse for two to six weeks, a square ulceration (u) is produced by a radium plaque or square red hot cautery. (E) Area of epilation due to benzpyrene solution. (2) Two weeks later the ulceration is partially healed. (U) Residual ulcer. (H) "Healing" epithelium. Benzpyrene applications have continued. 3 (S) Healed ulcer. (L) Papillomata and carcinomata have developed in skin *surrounding* site of ulcer.

developed in the skin about the burned area while the ulcers were still present, but healing rapidly. These papillomata were not close to the healing margin.

In a single case the first papilloma developed in the recently formed epithelium, over the ulcer, but as further study showed, it remained benign while carcinomata subsequently developed in the surrounding uninjured skin.

DISCUSSION.—Under the conditions of the experiments nonneoplastic squamous epithelium of the mouse's skin proliferating as a result of a "wound healing" stimulus, induced by radium ulcers and actual cautery burns, did not exhibit a marked susceptibility to malignant degeneration as a result of exposure to benzpyrene, a potent carcinogenic agent. Healing apparently took place uninfluenced by this agent, and ceased at just the proper time with no excess production of epithelial cells.

It might be pointed out that since benzpyrene requires a latent period of some 50 to 60 days for malignant degeneration to develop and since in the above experiments healing of the ulcers had occurred in 22 to 25 days, there was not sufficient time to permit the observation of a greater sensitivity on the part of healing epithelium. This point is answered by Experiment II where the wound healing stimulus was not induced until 45 days had elapsed since the beginning of benzpyrene application.

A greater sensitivity on the part of normal healing epithelium might have resulted in at least a majority of instances of papillomata first appearing in the healing margins or in the recently healed areas, or there might have been some evidence of piling up of epithelium at the termination of healing, such as a keratotic plaque or papilloma in the completely healed areas. Actually, only one papilloma out of a total of 40 lesions in eight animals (Experiment II) developed in the healing areas; the remaining lesions developed in the surrounding uninjured skin.

The above experimental results cannot be construed to indicate that there is little or no relationship between the stimulus to "healing" epithelium and the stimulus to epithelial neoplasia. This of course has not been demonstrated. However, one known carcinogenic substance of high potency was employed rather than a highly complex material such as tar. One large wound, which to heal required 25 to 30 per cent of the latent period for production of carcinoma in intact skin by this substance, was produced, rather than repeated injuries which might well induce a more complex series of tissue changes than obtains in a single healing wound. If the question of the relationship between trauma and repair (regeneration) on the one hand and neoplasia on the other hand is to be studied experimentally, it would seem that the initial observations should begin with the simplest experimental conditions. It was with this purpose in mind that the above experiments were undertaken.

The results described above are in accord with the recent observations of Reimann and Hall,[14] who found that the application of para-thio-cresol (which contains the natural cell "proliferating-stimulating group sulphydryl") in combination with 1, 2, 5, 6 dibenzanthracene did not reinforce the carcino-

genic action of the latter. In fact, it inhibited this, not by action upon the compound but by action upon the exposed cutaneous epithelium.

SUMMARY.—In a series of control mice one to two drops of 1 per cent benzene solution of 1:2 benzpyrene applied three times a week to the back induced multiple cutaneous papillomata and carcinomata after 50 to 65 days.

In another series of mice applications of an "unfiltered" radium plaque two weeks after beginning triweekly benzpyrene applications produced large (1 x 1 cm.) ulcerations in ten days. These healed in the course of 25 days, the benzpyrene applications being uninterrupted for 90 days after the first application. In a third group of mice actual cautery burns (1 x 1 cm.) were produced in the interscapular region 45 days after the first application of benzpyrene. These were also healed 25 days later.

The multiple papillomata and carcinomata produced in the latter two groups did not arise, except in two instances, in the proliferating epithelium at the margins of the healing ulcers or in the recently formed epithelium over the healed ulcers, but did develop in the surrounding uninjured skin.

Thus rapidly proliferating epithelium that finally covered the ulcers did not appear to be highly susceptible to the carcinogenic action of 1:2 benzpyrene. The wounds healed uninfluenced by the carcinogenic agent, whether they were produced early in the application of the latter or whether they were produced toward the end of the latent period necessary for the development of carcinoma in uninjured skin by this substance.

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A NEW METHOD OF PREPARING NONPYROGENIC INTRAVENOUS INFUSION FLUIDS *

BASED ON REMOVAL OF PYROGEN BY ADSORPTIVE FILTRATION

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Febrile reactions following intravenous injection of aqueous solutions have been known nearly as long as intravenous therapy itself. These reactions are characterized by fever, often chills, vomiting and other gastrointestinal disturbances. The fever begins 30 to 45 minutes after injection, reaches its height in two to four hours and then begins to recede until after four to six hours it has fallen to practically normal.

The literature on the subject was reviewed by Siebert[1] in 1923. Up to that time the only definitive observations were those of Wechselmann[2] and of Hort and Penfold.[3] Wechselmann, in 1911, showed that febrile reactions following the intravenous administration of salvarsan solutions could be eliminated if the solutions were made with distilled, germ-free water. This disproved the theory that the reactions were the result of a specific water or salt effect. Hort and Penfold in the same year found that water obtained by distillation from a Jena glass retort produced no fever if injected at once. However, a sample of the same water, autoclaved and allowed to stand at room temperature for 48 hours, produced marked fever. They further showed that there was no parallelism between the toxicity of water and the number of micro-organisms present; and that the "pyrogen" was contained in the supernatant portion of a centrifuged specimen and was filtrable through a Doulton filter, cotton wool, and even a Berkefeld filter. Siebert extended this work, identified a bacterium from distilled waters standing in nonsterile containers, showed that the pyrogen was the product of this organism but not identical with the bacterial bodies themselves, and that it was not retained by Berkefeld filters. She further showed that water distilled from an all-pyrex still equipped with a spray-catching trap and used within 24 hours was nonpyrogenic. Bourne and Siebert[4] subsequently identified two groups of river bacteria causative of this febrile reaction. They were Groups X and XI of Jordan, the latter group causing a milder reaction than the former. This work was confirmed by Banks in 1934.[5] Rademaker,[6] in 1930, stated that he confirmed Siebert's work and formulated a set of rules governing the preparation of infusion fluids. Perkins,[7] and recently Walter,[8] reported that infusion fluids prepared according to the specifications of

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Rademaker are nonreactive. It may be said that at present fluids are prepared according to the specifications of Siebert and Rademaker in most hospitals and commercial houses.

However, reactions still occur. While in the case of hospital-prepared fluids such accidents may be blamed on the oversights of an overworked staff, for fluids prepared in commercial houses there is no such excuse. Here mechanized and standardized methods of preparation are employed.

An analysis of the method of preparation recommended by Siebert and Rademaker shows the weakness of the method. It may be summarized in the following schema: Distillation ⟶ addition of chemical ⟶ sterilization of mixture.

Thus, while the distilled water may be of unquestioned initial purity, there is no insurance against contamination during the latter part of the preparation, that is, during the addition of chemicals and subsequent handling. A redistillation is out of the question and Berkefeld filtration is inefficient in removing the pyrogen once it is present.

The first part of this report deals with our attempts to remove the pyrogen by filtration through (1) a Jena filter; (2) a Berkefeld W filter; (3) Zsigmondy membrane ultrafilters of graded porosity; and (4) Seitz serum No. 3 filter pads made of compressed asbestos.

Table I embodies a study made on dogs.[9] The reactive infusion fluids were made from two lots of water: (1) A tap water from the city main incubated for 48 hours; (2) the water from a fresh water aquarium used in the laboratory. The water was boiled, filtered through hard filter paper, and sodium chloride was added to make a physiologic saline solution. It was then resterilized in the autoclave before injection. It should be noted that dogs' normal temperatures range from 100.6° to 102.6° F.

TABLE I

EACH OF THE EXPERIMENTS IN THE APPENDED TABLE IS REPRESENTATIVE OF AT LEAST FIVE EXPERIMENTS

Exp. No.	Kind of Water	Type Filter	Wt. of Dog, in Kg.	Vol. Injected Cc.	p_H	Temp. Changes in °Fahrenheit	Changes W. B. C. ×1,000	Symptoms
1	Tap		17	130	7.17	102.4–104.8		Shivering
2	Aq.		16	45	7.88	102.2–105.8	30.65– 6.4	Shivering, diarrhea
3	Aq.	Jena & Berk, W..	13.5	150		101.4–105.9		Shivering, diarrhea
4	Tap	Jena & Berk, W..	14	150		102. –105.2	20.5 – 7.8	Shivering, diarrhea
5	Tap	Seitz.....	15	250	7.02	102.2–101.8	17.8 –15.0	No symptoms
6	Aq.	Seitz.....	16.5	250	7.52	102.6–101.6	21.2 –20.8	No symptoms
7	Aq.	Zsig. 1 sec.....	13	250		102.1–105.3	10.2 – 4.8	Shivering, vomiting prostration
8	Tap	Zsig. 1 sec.....	14	250		102.0–104.6	12.8 – 6.4	Shivering, diarrhea
9	Tap	Zsig. 42 sec.....	15	250		101.8–104.2	10.6 – 5.3	Shivering
10	Aq.	Zsig. 42 sec.....	16	210		102.4–104.5	40.3 –12.75	Shivering, retching
11	Aq.	Zsig. 200 sec.....	16	325	7.61	101.8–101.4	17.05–16.8	No symptoms
12	Tap	Zsig. 200 sec.....	15.5	350	7.12	102.4–102.2	16.4 –14.8	No symptoms

W. B. C. = leukocytes
Aq. = aquarium
Berk. = Berkefeld W
Zsig. = Zsigmondy

In this study a number of precautions were necessary. They were occasioned by the fact that in clinical circles, in addition to the presence of pyrogen in infusion fluids, it has been alleged that a number of other factors cause febrile reactions. These have accumulated without any conclusive proof or disproof of their validity. The precautions, pertinent to this investigation, were: (a) The p_H of the fluid;[10, 11, 12, 13] (b) contamination by the rubber tubing through which the fluid is administered;[8, 9, 10, 13] (c) the temperature of the injected fluid;[10, 13] and (d) the speed of the injection.[10, 11, 13]

Accordingly, the p_H of the fluid was taken before and after filtration, the rubber tubings used were two foot lengths of gum tubing which had been repeatedly used for other infusions previously and were thoroughly rinsed with sterile distilled water and autoclaved before each use, the fluid was maintained at 39° C. throughout the injection and the speed of injection was in each case regulated by gravity or gravity plus air pressure to .5 cc. per kilogram body weight per minute, *i.e.*, the equivalent of 900 cc. per 30 minutes for a 60 Kg. man. The temperatures were taken at half-hour intervals for a period of five hours. Only two leukocyte counts were made as a rule, one before and the other 45 minutes after injection.

Experiments 1 and 2 are the controls. It will be seen that 45 cc. of the aquarium water produced more of a reaction than 130 cc. of the tap water. Experiments 3 and 4 show that neither a Jena crucible nor a Berkefeld W filter, the finest obtainable, removes the febrile agent. This finding confirms that of Hort and Penfold and of Siebert. Filtration through Seitz serum No. 3 filter removes it, however, as may be seen in Experiments 5 and 6. Since Seitz filters act by adsorption, the conclusion from these experiments is that the pyrogen is adsorbable. Experiments 7 to 11 are attempts to determine the particle size of the pyrogen. Since it passes through a 42-second filter but is held back by a 200-second filter, it is concluded that the particles lie between one micron and 50 Mμ.*

Table II shows four representative series of experiments on human beings.

The first series dealt with a commercial 5 per cent glucose solution. The protocol of patient L. T. was taken from the hospital record. It will be seen that the temperature rose from 98.4° to 102.6° F. Four hundred cc. of the same solution were given to an 11 Kg. dog, resulting in a marked temperature rise and leukopenia. One thousand cc. of the same fluid filtered through a 200-second Zsigmondy membrane filter gave no reaction to the patient. Through one layer of Seitz No. 3 filter, 600 cc. still gave a slight fever, but 1,000 cc., after filtration through two layers of Seitz No. 3 filter, was followed by no temperature rise.

Series II was performed with a commercial glucose solution from another

* From data supplied by the manufacturer.

TABLE II

Series No.	Fluid	Subject	Vol. Injected Cc.	Filter	p_H	Temp. Changes in ° Fahrenheit	Changes W. B. C.
I	Dextrose Com. Lot A Solution—5%	(a) Patient L. T.....	250	0	6.30	98.4–102.6	8,600– 6,200
		(b) Dog (11 Kg.).....	400	0		101.6–106.0	17,050– 2,250
		(c) Patient V. H.....	1,000	Zsigmondy M 200-second	6.50	99.4– 99.6	14,500– 9,100
		(d) Patient A. S.....	600	Seitz once		99.2–100.8	12,000– 8,000
		(e) Patient T. N.....	1,000	Seitz twice	6.85	99.0– 99.4	8,500– 8,000
II	Glucose Com. Lot B Solution—10%	(a) Patient R. S.....	150–200	0	4.10	99.6–104.8	
		(b) Dog (13 Kg.)	100	0		101.2–104.6	21,830–13,400
		(c) Patient C. D.....	500	Z-M 200-sec.	5.61	98.8– 99.6	12,200– 8,900
		(d) Patient P. S.....	1,000	Seitz twice	6.61	98.6– 99.2	11,000–11,500
III	(Tap) Water Saline	(a) Volunteer M. S...	125	0	7.71	99.0–102.4	10,000– 6,000
		(b) Volunteer.....	1,000	Z-M 200-sec.	7.12	99.2– 99.0	8,000– 7,800
		(c) Volunteer.....	1,000	Seitz twice	7.02	98.6– 98.8	7,500– 7,800
IV	Aquarium Water Saline	(a) Volunteer A. P....	40	0	7.88	99.4–103.8	10,000– 5,000
		(b) Volunteer.....	1,000	Z-M 200-sec.	7.61	98.6– 99.0	8,300– 9,200
		(c) Volunteer.....	1,000	Seitz twice	7.52	98.8– 98.8	16,000–15,200

manufacturer. Series II and III were saline and aquarium water used on the dogs in Table II. The toxicity of the tap water is shown in the experiment in which 40 cc. of it, in a human being (A.P.), caused a temperature of 103.8° F. and a fall of the leukocyte count of from 10,000 to 5,000. The lack of reaction when 1,000 cc. each of the filtrate of the same water is injected after filtration through the 200-second Zsigmondy and through Seitz attests the high efficiency of these methods of filtration and confirms the findings in dogs.

The leukopenia accompanying this reaction is invariably present in dogs as may be seen in Table I, but is less constant in human beings, although in human cases where the reaction is marked, it is unmistakable and has even reached a level as low as 900. This is a transient phenomenon, most marked in the first hour or two, with restoration to normal in a few hours. This phenomenon will be the primary subject of a subsequent study.

It will be seen from the p_H values recorded in Tables I and II that they range from p_H 4.10 to 7.88 for reactive fluids and from 5.61 to 7.52 for nonreactive fluids. Under these conditions then the p_H value *per se* cannot be the cause of the reactions caused by these fluids.

Discussion.—The theoretic implication of this work is that the pyrogen found in infusion fluids is of a particulate nature, of the order of magnitude of from 50 Mμ. to one micron. Whether it is of protein or of other composition, whether it acts as a particle *per se* or in some other way; and whether other particulate substances of this dimension can reproduce this phenomenon remains to be investigated. This finding is not necessarily at variance with Siebert's. It is easily conceivable that the products of the *Bacillus pyrogens* could occur as particles of this size.

The practical result of this work is that there are now available two processes of filtration which effectively remove the reactive agent from infusion fluids. One is ultrafiltration which, however useful it may be in the determination of particle size, is too slow and technically difficult for clinical use. The other process is adsorptive filtration through two layers of Seitz serum No. 3 pads (compressed asbestos). This process is easy to manipulate and should be feasible for the use of hospitals and commercial houses. In this process neither distillation of the water nor a final sterilization by heat is essential, although both are recommended—the former because on general principles it is best to use water free of chemicals other than those prescribed, and the latter to avoid bacterial contamination during bottling. This new process of infusion water preparation may be summarized by the schema: Distillation ⟶ addition of chemicals ⟶ adsorptive filtration ⟶ sterilization.

While in the old processes there may be said to be only one "purifying" step: namely, the distillation of water, in this new process there are two: Distillation at the beginning and adsorptive filtration at the end.

SUMMARY

In a study with infusion fluids known to be fever-producing, it was shown that:

(1) The fever producing agent is removal by an adsorptive filter and by ultrafiltration through a 200-second Zsigmondy filter.

(2) The agent is of a particulate nature of the order of magnitude of 50 Mμ. to one micron.

(3) A new method of infusion fluid preparation is described. It consists of passing the final fluid mixture through compressed asbestos filters of the Seitz EK type.

The authors wish to acknowledge the help of Dr. Benjamin Shafiroff and the unfailing encouragement and advice of Professor Arthur M. Wright. The ultrafilter was loaned to us through the courtesy of Dr. E. Lowenstein of the Pfaltz and Bauer Company.

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BRIEF COMMUNICATIONS AND CASE REPORTS

PANCREATIC CYSTS

TREATED BY OPERATION IN CONJUNCTION WITH A SCLEROSING AGENT

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IT IS not my purpose to discuss pancreatic cyst other than to describe a procedure which I have used in one case and which I have never seen described in the surgical literature, nor do I know of its ever having been employed before. Although a review of the literature indicates that pancreatic cysts are comparatively infrequent, they do occur frequently enough to deserve our consideration in interpreting any upper abdominal symptomatology.

The most frequent treatment of pancreatic cysts has been either by drainage and marsupialization or complete excision. Neuffer[1] has suggested pancreaticocholecystostomy. The objection to treatment by marsupialization and drainage is the prolonged drainage and the possibility of a permanent fistula. The procedure of extirpation, or excision, is usually not practical and the operation is too formidable.

Recently a patient with a large pancreatic cyst was referred to me. It was considered that, at the time of operation, by employing a sclerosing agent, such as is used in the treatment of varicose veins, it might be possible to sclerose and obliterate the cyst, thus preventing the usual prolonged drainage and probably obtain in the end a more permanent cure without recurrence.

Case Report.—A white male Hebrew, age 50, was admitted to the Jackson Infirmary, February 23, 1936. His past history, until a few months before admission, was unimportant. At that time the patient began having vague digestive upsets and complained of fulness and discomfort in the upper abdomen. He had consulted various doctors who had diagnosed and treated his condition variously as cirrhosis of the liver, chronic cholecystitis, chronic appendicitis, hyperacidity and malignancy of the stomach.

Present History.—Two months ago the patient was admitted to the Jackson Infirmary complaining of an acute pain in the upper abdomen. At this time a tentative diagnosis of acute cholecystitis was made. However, before he could be operated upon, he developed pneumonia. The operation was deferred and the patient treated primarily for his pneumonic condition. He was discharged at the end of two weeks, at which time his abdominal symptoms had subsided. One month later the abdominal pain returned and he consulted an internist in New Orleans, La., remaining under his observation for some time. During this period, there was present a large, tender mass in the upper abdomen. A diagnosis was made of cirrhosis of the liver, and a

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dietary regimen instituted. The mass in the upper abdomen became more noticeable and the pain more severe. He was admitted to the Jackson Infirmary, February 23, 1936.

Physical Examination.—The abdomen contained a large, symmetrical, smooth, movable, soft mass which occupied the epigastric region. The tumor was very tender and felt to be about the size of a grapefruit. It was not connected in any way to the liver. The abdomen, except in this region, was apparently negative for any other pathology. Temperature 100° F.; W.B.C. 15,000; polymorphonuclear count 82 per cent. Uranalysis was negative except for positive sugar. Roentgenologic examination showed: "An apparent cholecystitis, with periduodenal and pericolic adhesions and an appendicitis." The examination demonstrated that the mass was not connected with the stomach or the colon. Except for the sugar in the urine and the location of the tumor, there was nothing to suggest any pancreatic involvement.

Operation.—Through an upper right rectus incision, a large mass was disclosed situated between the stomach and the transverse colon behind the gastrocolic omentum. The gastrocolic omentum was opened and a large, soft, cystic mass presented. Its contents were aspirated and found to consist of about 150 cc. of a dark, grayish-black, thin fluid. The cyst was incised and on exploration it proved to be connected with the midsegment of the pancreas. The lining membrane of the cyst was inflamed and partly gangrenous. Its external surface was very adherent to the surrounding structures. A complete excision of the cyst was, therefore, not attempted, nor was it deemed advisable. A small rubber tube was inserted into the cavity of the cyst and around this, gauze saturated with sodium morrhuate was packed. No attempt was made to suture the edges of the cyst wall to the peritoneum. The wound was closed about the tube and the gauze pack.

Postoperative Course.—Two days postoperative, 5 cc. of sodium morrhuate were injected through the drainage tube. This was repeated on the following day. On the fourth day, gradual removal of the gauze pack was begun and its complete withdrawal accomplished on the tenth day. The sutures were removed on the eighth day. The patient was discharged on the eighteenth day with the wound entirely healed.

Follow-up.—During the past year, the patient has been entirely well, has had no digestive upsets and there has been no return of the tumor. The sugar has completely disappeared from his urine.

COMMENT.—By employing a sclerosing agent in conjunction with the surgical procedure, I believe the long period of drainage which usually accompanies these cases was prevented. The patient seems to have completely recovered and there has been no recurrence of the cyst.

Although I have not tried the procedure, it is my opinion that in a case presenting a chronic pancreatic cyst, where there is no acute inflammation, where a diagnosis can be definitely made, and the contents of the cyst aspirated, it would be entirely possible and safe to fill the cavity of the cyst with a sclerosing agent, such as sodium morrhuate or quinine hydrochloride, without the necessity of undertaking a major surgical procedure. However, I believe in most cases surgery combined with the employment of a sclerosing agent is probably a safer and a saner method of treatment.

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ACUTE INTESTINAL OBSTRUCTION DUE TO A MESENTERIC DEFECT

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THE passage of a loop of intestine through a defect or hiatus in its mesentery is considered to be one of the most uncommon of the many different mechanisms capable of producing acute intestinal obstruction. Reviews of the literature by Cutler[1] and Edwards,[2] and recent case reports by King,[3] Cullen[4] and Bennett,[5] have yielded a total of only 37 cases. It was an unusual coincidence that the following case came under my observation just two weeks after the publication of Cullen's article.

Case Report.—A colored male, age 30, entered the Passavant Hospital, March 31, 1936, complaining of excruciating abdominal pain of one and one-half hours' dura-

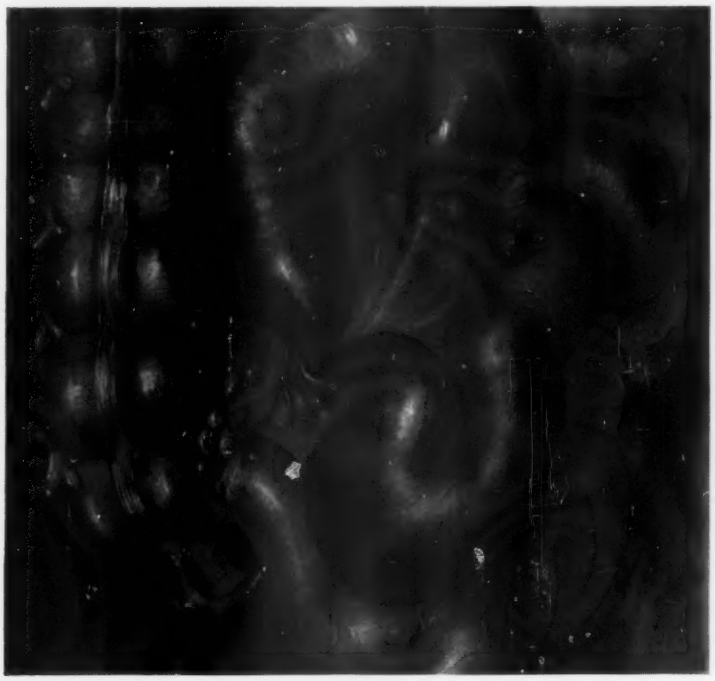

FIG. 1.—Illustrating the situation and general anatomic relations of the herniated terminal ileum through the hiatus in its mesentery.

tion. He stated that for the last nine years he had had distress after meals, consisting of nausea with occasional cramps and vomiting. One of these symptoms or a combination of them would occur almost daily with the exception of infrequent free periods of from three to four days. The cramps were always localized in the region of the umbilicus and were never followed by residual tenderness. For the same

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duration of time he had noticed increasing constipation which he corrected by taking salts or milk of magnesia three or four times a week.

He had had influenza and pneumonia in 1917, and a chancre in 1925, for which he received two courses of treatment. There was no history of previous injury or operation.

One and one-half hours before admission to the hospital he was awakened out of a sound sleep by severe abdominal pain which was cramping in character and extended over the entire abdomen. The pain was constant and was so severe that

FIG. 2.—Illustrating the anatomic relations at the conclusion of the operative procedures.

he could find no position in which he was comfortable. He became nauseated and vomited shortly after the onset, the latter becoming increasingly more frequent as the attack persisted.

Physical Examination revealed a well developed and well nourished man, obviously suffering from extreme pain and vomiting small amounts of bile-tinged fluid at frequent intervals. There was evidence of shock. The skin was cold and clammy. Temperature 96.8° F.; pulse 50 and of poor quality; respirations 46; blood pressure 70/40. All other abnormal findings were limited to the abdomen. There was generalized tenderness, being somewhat more marked on the right side, especially in the right lower quadrant, accompanied by considerable voluntary spasm which was replaced by a peculiar doughy resistance when the patient relaxed. There were no palpable organs or masses. Rectal examination was negative.

Laboratory Data.—The urine was negative. White blood cells 17,700 with 76 per cent lymphocytes and 24 per cent polymorphonuclear leukocytes.

The diagnosis was indeterminate, although there was no doubt as to the presence of an acute intra-abdominal lesion demanding early intervention. The patient was operated upon three and one-half hours after the onset of symptoms.

Operation.—Abdominal exploration through a right midrectus incision revealed a loop of strangulated bowel which was about 150 cm. in length. This was found to consist of the entire lower ileum except for the distal 6 cm., and had been produced by the passage of the loop through a hole in its mesentery. The defect in the mesentery was situated about 6 cm. proximal to the ileocecal valve, was about 1 cm. in diameter and had a tense fibrous border which had to be divided before reduction could be effected (Fig. 1). After reduction there was evidence of gradual improvement in the circulation of the loop except for the distal 42 cm. which remained dark and lusterless, and which was finally resected up to within 4 cm. of the cecum. The ends of the ileum were then closed and intestinal continuity reëstablished by means of a side-to-side ileocecostomy. The appendix was normal and was not removed. A Witzel enterostomy was performed proximal to the anastomosis and the incision was closed (Fig. 2).

The patient had a stormy convalescence with persistent abdominal distention despite the fact that he was passing flatus and liquid stools both by rectum and through the enterostomy tube. Further decompression was obtained by means of Wangensteen's continuous suction syphonage, and his condition seemed to improve until the eighth day after operation, when the enterostomy tube ceased to function. This was followed rapidly by an increase in the abdominal distention and a rise in the pulse rate. A second enterostomy was performed through a low left gridiron incision under local anesthesia, the tube being inserted in the first loop of distended bowel that presented. Following this procedure he showed definite and continued improvement, finally leaving the hospital 36 days after admission with both incisions healed and with his bowels moving regularly with the aid of mineral oil.

He has been seen at intervals since his discharge, and has repeatedly volunteered the information that he feels fine and has had no recurrence of the distress which he formerly experienced after meals.

It is difficult to explain the etiology of mesenteric defects, and in the absence of any suggestive cause many of them have been thought to be congenital in origin. Rupture of the mesentery from external violence and injury to it during the course of a previous operation have been considered as possible causes and cannot be excluded where a history of previous trauma or operation exists. King has recently advanced the theory that they may be the result of an antecedent inflammation of the appendix with involvement and subsequent atrophy of the mesentery, and he reports one case in which this sequence seemed to be clearly demonstrated.

The etiology of the defect in the case herewith cited is obscure. There was no history of trauma or operation. There was no history of acute appendicitis, and although the appendix was not removed, its gross appearance was normal. The defect had apparently been present for a long period of time, and in view of the complete relief which the patient experienced following operation, had probably been responsible for the vague gastro-intestinal symptoms which he had experienced during the previous nine years.

The treatment is similar to that of any other hernia in which there has

been strangulation of the intestine. Simple reduction and repair of the defect is the procedure of choice although resection may be necessary if the circulation to the involved loop has been badly compromised. The mortality varies with the procedure, Edwards finding 11 recoveries in 13 cases in which reduction was effected and four recoveries in eight cases in which resection was necessary. Since the publication of his paper, King and Bennett have each reported one case of reduction with recovery, while Cullen has reported one case in which resection was successful.

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ANGIOMA OF THE SKULL

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ANGIOMA of the skull is not a common condition, as a careful review of the literature reveals only a few cases. Angioma of the bone is found most frequently in the vertebrae and occasionally in flat bones—such as the sternum, scapula or skull. The two types of angioma of the bone are cavernous and capillary. The cavernous type of angioma is one in which there are large spaces filled with blood, resembling a cavernous angioma found elsewhere in the body. The capillary type is one in which there are many small openings filled with blood and interspaced with a great deal of fibrous tissue. Toynbee,[1, 2] in 1845, first described an angioma of the skull, and since then 18 authors have referred to angiomata of the skull. Table I contains a brief résumé of the type of angioma and associated lesions reported by the various authors.

In only a few of these instances was surgery attempted, and the following case is comparable to one described by Geschickter,[19] who reported a congenital angioma excised from the skull and scalp of a girl, aged 17 months, in which the inner table of the skull was intact.

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TABLE I

RÉSUMÉ OF ANGIOMATA AND ASSOCIATED LESIONS REPORTED BY VARIOUS AUTHORS

Author	Age	Sex	Location	Remarks
Toynbee[1,2]	19	M.	Parietal bone	Died of tuberculosis
Ehrmann[3]	40	F.	Left parietal bone	Removal. Died of meningitis
Cruveilhier[4]	38	F.	Twelve angiomata of skull; one of femur; one of third rib and of both shoulders	No detail given
von Rokitanski[5]			Angioma of parietal lobe	None
Morris[6]			Right parietal bone eroded the skull	Removal
Stamm[7]	4 mos.	F.	Angioma skin, muscles, bone, kidney, ovary, lungs, brain and skull	Found at autopsy
Pilcher[8]			Angioma vault of skull	Removed
Ziegler[9]			Angioma of skull	
Zajaczkowski[10]	38	F.	Frontal bone	Removal. Tumor pulsated in the center
Schöne[11]	39	M.	Angioma occipital bone	Removal with recovery. Tumor pulsated in the center
Major and Black[12]	34	M.	Angioma each temporal bone	Also angioma liver and bilateral cystic adrenals found at autopsy
Brandt[13]	47	M.	Angioma left petrous bone	Found at autopsy; also angioma retina of right eye, cerebellum, cauda equina, kidneys, pancreas, spleen and questionably in the long bone. This was a report of Von Hippel's case
Kaufman[14]	76	M.	Angioma of skull	Found at autopsy
Cushing[15]	26	F.	Right parietal bone	Successfully removed
Lanari and Marque[16]			Two cases of angioma of the skull	Treated successfully with roentgen ray
Erös[17]	70	F.	Angioma of frontal bone. In addition, multiple small angiomata of other cranial bones	Found at autopsy
Overend[18]		M.	Angioma occipital bone	Demonstrated by roentgen ray and removed
Geschickter[19]			Five angiomata of skull	One congenital angioma removed from skull and scalp of a 17 mos. old female. Inner table of the skull intact

Case Report.—D. T., female, age 3, referred by Dr. C. V. Edwards of Council Bluffs, Iowa. The child had a normal birth and the rate of development was uneventful. However, from birth it was noted that there was a defect in the right frontal region which would become larger when the child was reclining and smaller when it was in an upright position. The baby had a tendency to cry out sharply in the night. When two years of age, roentgenograms were taken and it was felt that the child was suffering from an encephalocele. Examination, June 23, 1936, revealed a well developed and nourished child 39½ inches tall, weighing 35 pounds. There was a bulging area in the right frontal region, and palpation of this mass revealed the content to be filled with fluid. Auscultation failed to reveal a bruit. When the child would recline, the mass would become enlarged and, upon assuming the upright posi-

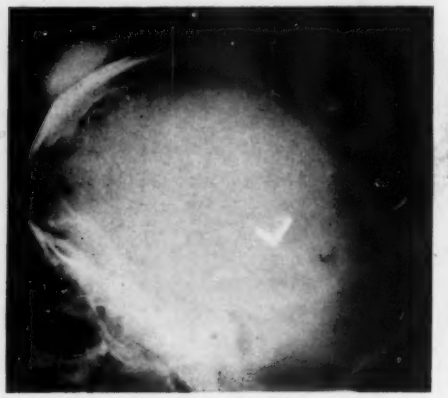

FIG. 1.—Roentgenogram showing the bulging mass over right frontal region and small line in skull.

FIG. 2.—Roentgenogram showing the bulging mass and destruction of the skull in the right frontal region.

tion, it would become somewhat smaller. Other than the presence of large, cryptic tonsils, examination was essentially negative, as were laboratory tests of the blood and urine, including the Wassermann reaction. Roentgenograms revealed a bulging mass in the right frontal region with a small line in the skull which might suggest an encephalocele.

The child was admitted to the neurosurgical service of Mercy Hospital and an attempt was made to reduce the size of the mass by spinal drainage. However, the spinal fluid pressure was 8 cm. of water, and withdrawal of 30 cc. of cerebrospinal fluid failed to affect the size of the mass. On June 26, under avertin anesthesia, a needle was introduced into the mass and bloody fluid was aspirated. A hockey stick incision was then made around the mass, which was the size of a large frankfurter, measuring 10 x 4 cm. The skin was dissected off and a tumor mass was found to be attached to the skull and covered with periosteum. On carefully dissecting this free, many small veins were seen to be communicating with this mass and the inner table of the skull, which was found to be intact. The mass had completely replaced the outer layer of the skull. After its removal the bleeding from the bone was controlled with bone wax. A perforator opening was then made into the inner table of the skull but no tumor tissue was found below. The bare area was covered with periosteum, as shown in Figs. 3 and 4, and the wound was closed in the usual manner.

The child made an uneventful recovery and was discharged from the hospital in ten days. Pathologic examination of the tumor showed it to be a fibrous angioma of the skull.

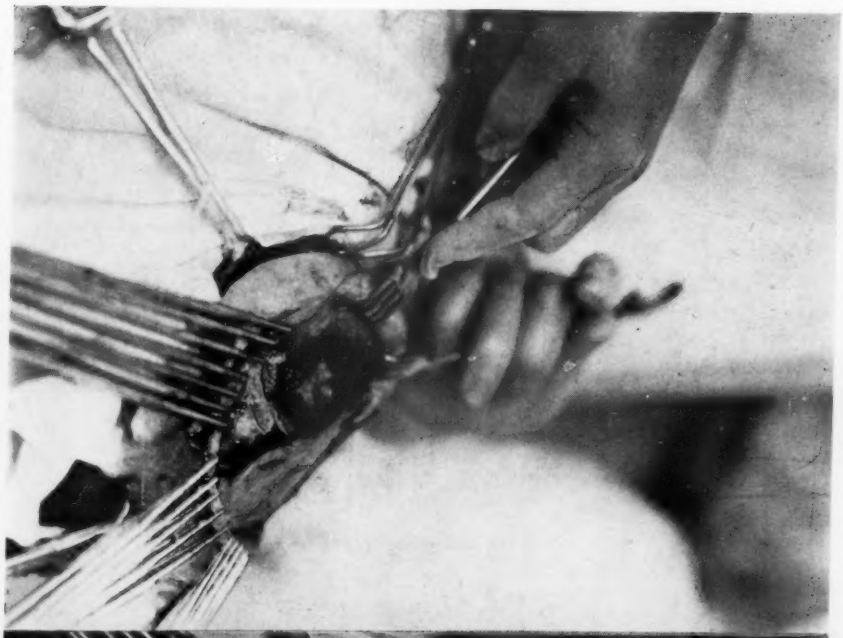

FIG. 3.—Photograph of angioma taken at operation.

FIG. 4.—Photograph of the inner table of the skull intact, after removal of the angioma.

A letter from the child's parents, February 26, 1937, stated that the little girl was developing normally and that there was no evidence of recurrence of the tumor.

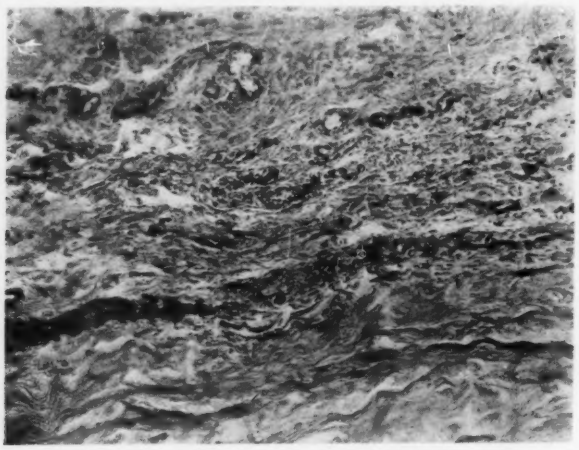

FIG. 5.—Photomicrograph of the tissue removed, showing a capillary angioma containing a marked amount of fibrous stroma (×100).

CONCLUSION

Angioma of the skull is an unusual condition which is amenable to extirpation if care is exerted in the control of hemorrhage during operation.

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ADVANCEMENT OF THE RECEDING LOWER JAW

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Micrognathia or a diminutive or short mandible presents in its correction a number of troublesome surgical and dental problems. To enlarge the arch of the lower jaw by step-shaped sections and separation of the bone is a serious operation, prone to be complicated, when attempted as a submucous procedure, by penetration into the mouth and consequent infection of the bone, and a prolonged period of suppuration and sequestration. Even advancement of the mandible by division of the rami entails weeks of immobilization, difficulty at times in obtaining union and, if the section is made below the spine of Spix, division of the inferior dental nerve and vessels. In any case the aid of an expert orthodontist is very desirable to obtain the best possible occlusion of ill matched upper and lower teeth. For the average patient attempts to improve the occlusion of the teeth and to improve the personal appearance of the patient by correcting the receding chin or "bird face" have been the only procedures that seemed justifiable. Through an incision, concealed by being placed below the symphysis menti, a pocket is formed in which are embedded masses of cartilage or fat of a size appropriate to advance the contour of the chin. At times extraction of residual and useless lower teeth with the insertion of lower denture of a more massive type is used not

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only to improve the power of mastication, but also the personal appearance. For extreme micrognathia an operation upon the lower jaw is justified by the deformity and disability.

Recently as I was about to divide both rami of a receding jaw, in order to produce an advancement to match the superior maxilla, it was decided to try the effect of merely advancing the temporomandibular articulations. Each joint was therefore exposed by an incision carried along the anterior border of the ear. Above, the incisions were angled forward and upward above the zygoma to place the scar above the hair line and to avoid injury to the upper branches of the facial nerve. On each side the flap of skin with the external maxillary vessels was retracted forward and downward; the zygoma resected and the eminentia articularis removed by a small sharp chisel. The articular head of the mandible with its extensive articular capsule was readily displaced forward by pressure with a periosteal separator, and the removed segments of zygoma and eminentia inserted in the space thus opened behind the articulation. This advanced the lower jaw about 8 Mm. The wounds were closed and there was little secondary disability. The jaw could be opened and closed without difficulty, but the advancement of the mandible was insufficient and it was evident that 10 or 12 Mm. more were desirable. It was then realized that the insertion of quadrilateral sections of costal cartilage behind the advanced temporomandibular articulations would enable a simpler type of operation and the use of a shorter and less conspicuous incision. Therefore, about seven days later the wounds were reopened under local anesthesia, the inserted loose portions of bone removed and quadrilateral sections of the sixth and seventh costal cartilages, about 20 Mm. long, were inserted back of the advanced temporomandibular articulations. The wounds were again closed. Little reaction or discomfort followed. The patient was permitted to masticate food after the fourth day, which was accomplished without difficulty. The patient was discharged from the hospital ten days after the last operation.

The operation is effective, simple and produces but slight disability. With the knowledge gained from this patient, it was evident that a short incision without resection of the zygoma or articular eminence is all that is required. The incision should be vertical and accurately placed along the anterior margin of the external ear. If sufficient room is not obtained, the incision may be extended upward and curved slightly forward above the hair line. When such an incision is accurately united, the resulting scar is inconspicuous. Very fine (No. 35 B and S gauge) annealed, rustless steel wire introduced by a very fine curved needle produces the least tissue reaction. The incision lies behind the facial vessels and branches of the facial nerve. As the mandible is pushed forward by a thin, blunt instrument or Trousseau dilator, the cartilage is inserted immediately in front of the auditory meatus, the posterior surface of the cartilage being against the bony meatus. After the operation,

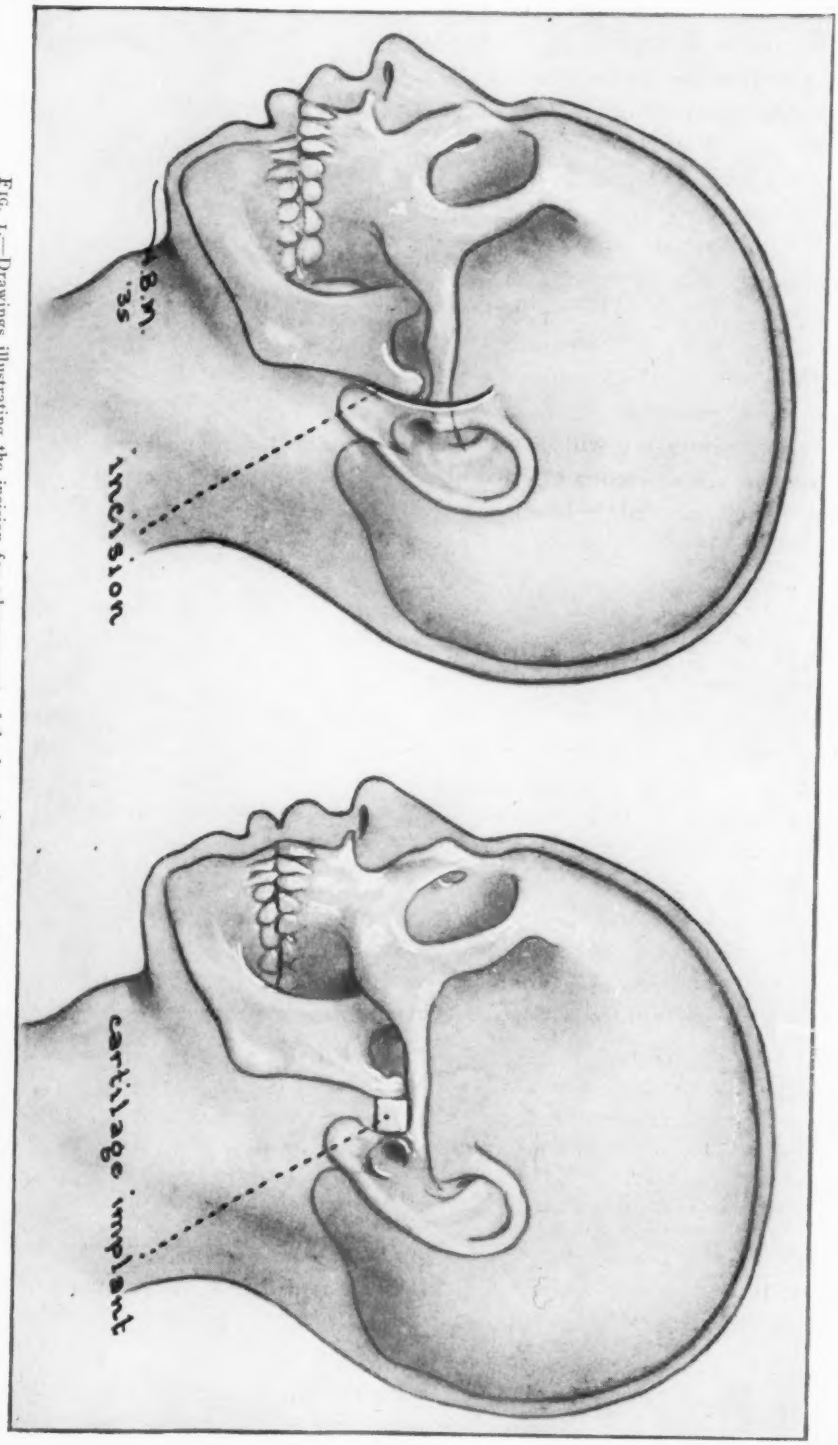

FIG. 1.—Drawings illustrating the incision for advancement of the lower jaw and the situation of the cartilage implant used.

the occlusion of the teeth may be improved by orthodontic measures. In certain cases an additional plastic operation upon the chin may be indicated to further improve the cosmetic result.

In any case, before any operation is attempted, an articulated model of the teeth is desirable as a guide to the best procedure and to the length of advancement.

EXOSTOSIS OF THE SCAPULA

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AN EXOSTOSIS of the scapula, with no similar lesions elsewhere, has been reported to be comparatively rare: Du Mortier and Halpert,[1] in 1934, reported two cases, and were able to find only 18 other instances in the literature.

Case Report.—Mrs. J. M., a white female, age 27, at the time of admission to Hermann Hospital, November 20, 1934, complained of loss of weight, a general "bad feeling" and that her right shoulder blade was out of place. In 1928, the patient noted that her right shoulder blade was prominent and she continually raised her right arm to try to put the shoulder blade back in place. This condition became more pronounced recently when she lost nine pounds of weight. There were a dull ache in the region of the upper arm muscles and another pain localized to the chest at about the level of the fourth rib, slightly to the right of the sternum. The latter pain was intensified by deep breathing.

Examination.—The patient was a thin woman and appeared chronically ill. Weight 106 pounds. The right scapula was displaced to the right about two inches from the normal position. It moved freely with movement of the right arm. A nodular mass on the axillary border of the scapula could be palpated with difficulty as the mass appeared to arise from the costal surface of the scapula. Roentgenologic examination showed a rounded, hen's egg-sized, bony tumor on the costal surface of the scapula near the axillary border at about the center of its length (Fig. 1). The rest of the thoracic cage and the long bones showed no departures from the normal. General examination revealed nothing more than a chronic bilateral otitis media and visceroptosis.

Operation.—Under general anesthesia, Dr. J. L. Taylor made an incision through the skin paralleling the axillary border of the scapula and exposed the tumor by blunt dissection. It was found to be attached by a pedicle and was chiseled off. The wound was closed and the patient made an uneventful recovery.

Pathologic Examination.—Dr. Violet H. Keiller reported the gross specimen as a cancellous osteoma with a cartilaginous cap. It was of mushroom shape, 5.2 cm. in its greatest diameter and 5.3 cm. at its greatest height. The base of the pedicle was 3 cm. and the height of the pedicle 0.6 cm. The cartilage cap was 0.3 cm. thick in some areas (Figs. 2 and 3). Sections of decalcified bone and its cartilaginous cap were made and showed typical cancellous osteoma with no evidence of malignancy. Examination of patient one year after operation revealed no other bony tumor or recurrence of the one removed. The functional result was good.

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FIG. 1.—Roentgenogram showing position of exostosis.

FIG. 2.—Photograph of gross specimen of osteoma of scapula. Note cartilage cap.

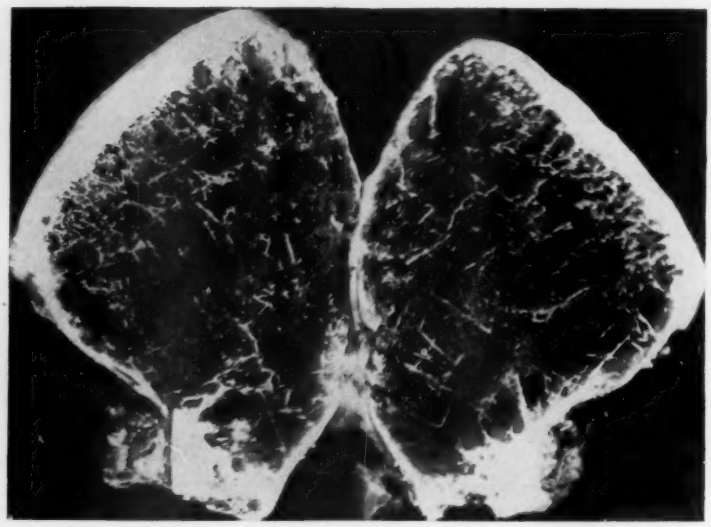

FIG. 3.—Photograph of section through middle of specimen showing the cancellous texture, thin, dense cortex and well defined pedicle.

TABLE I

REPORTERS OF OTHER CASES FROM THE LITERATURE

Condensed from Du Mortier and Halpert

Doctor	Date	Age	Sex	Location
(1) Beaumont	1836	13	M.	Inferior angle, right
(2) Pepper	1867	16	M.	Costal surface close to posterior border, right
(3) Birkett	1868	12	M.	
(4) Birkett	1869	16	F.	
(5) Birkett	1869	16	F.	
(6) Richet	1885	12	M.	
(7) Heurtaux	1885	24	M.	Attached to spine
(8) Von Kölliker	1891	10	M.	Medial angle of the right
(9) Von Kölliker	1891	4	M.	Medial angle of left
(10) König	1893	9	F.	Inferior angle, costal surface
(11) Robinson	1899	9	F.	Right inferior angle, costal surface
(12) Iribarne	1900	8	F.	Vertebral border posterior surface, left
(13) Gantcheff	1901	7	M.	Left vertebral border, costal surface
(14) Ferbas	1906	15	F.	Right vertebral border
(15) McWilliams	1914	18	F.	Vertebral border, costal surface, left
(16) Peak	1914	7	F.	Right costal surface
(17) Brown	1916	16	F.	Right costal surface, medial angle
(18) Genevrier	1923	12	M.	Right
(19) Du Mortier and Halpert	1934	7	M.	Left costal surface, inferior angle
(20) Du Mortier and Halpert	1934	16	F.	Right medial angle, costal surface

Discussion.—An osteoma of the scapula in a woman, age 27, is reported because of the infrequency of this condition. Only 20 cases were found in the literature. All except one had been discovered before the age of 20; both sexes are equally affected and either scapula may be the site of the lesion (Table I). Osteomata are believed to arise from accessory centers of ossification.

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POSTERIOR DISLOCATION AT THE ELBOW WITH RUPTURE OF THE RADIAL AND ULNAR ARTERIES

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DISLOCATION at the elbow is a condition commonly encountered, and is in frequency second only to that occurring at the shoulder.[1] Furthermore, luxation posteriorly is quite the most commonly observed type of displacement.[2] Special interest, however, in the case to be reported, lies, not in the

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primary diagnosis, but rather in the occurrence of a relatively rare vascular complication; namely, rupture of the radial and ulnar arteries.

Case Report.—I. S., a white male, age 20, while exercising, November 9, 1935, fell on his outstretched right arm. There resulted a posterior dislocation of the elbow with immediate local swelling. Reduction was effected under fluoroscopic control with some subsidence of swelling and pain. A few hours later the swelling again increased and pain became worse. At the time of admission, six hours after the injury, the boy's fingers had become numb and the numbness was extending up the arm.

Physical Examination.—The right arm, which had been immobilized at the elbow by an internal right-angle splint and carried in a sling, was swollen from the finger tips to the shoulder. The hand was blue and cold and no radial pulse could be felt (it was reported authoritatively that this had been felt immediately following the reduction). There was complete loss of sensation in the hand with progressive improvement in sensation up the arm to apparent normal a few inches above the elbow. Although the swelling at the elbow was very tense, it gave a sense of fluctuation. The inner surface of the upper arm was ecchymotic and there was a small abrasion on the inner aspect of the elbow. There was obviously present a surgical emergency.

Operation.—An incision was made over the swollen discolored area on the inner side of the elbow. A large hematoma was evacuated. The radial and ulnar arteries were then found completely severed just below the bifurcation and were bleeding freely. The severed ends of both arteries were ligated. In addition the muscles of the forearm at their attachment to the internal epicondyle were found to be almost completely torn across. The ends were approximated with catgut. The median nerve was visualized and found to be intact. The deep fascia and skin were left open to minimize the chances of further swelling. The arm was dressed on an internal right-angle splint.

Immediately following evacuation of the clot the color of the hand improved. The numbness previously present gradually disappeared over a period of several days. At the time of discharge, November 19, 1935, ten days after the injury, the color of the hand and arm was good, although there was still some swelling present. The radial pulse could not be felt. Sensation was normal. The wound was healing satisfactorily. Roentgenologic examination had revealed a complicating fracture of the head of the radius with the fragments in good position. On examination, December 14, 1935, the wound was completely healed and physical therapy was instituted. At this time extension at the elbow was distinctly limited.

Follow-up.—Objectively very little residuum of the injury could be demonstrated. Only by a comparison with the other arm could it be seen that extension of the elbow as well as the rotary movements of the forearm were very slightly limited—not more than five to ten degrees. Power and sensation (as tested by pin prick) were normal. The radial pulse had returned and was easily palpable. From the patient's point of view, restoration of function was complete.

Discussion.—Many of the standard reference books fail to even mention rupture of the large arteries as a possible complication of posterior dislocation at the elbow. Cotton[2] says that tearing of the brachial artery belongs with the complications of the rare compound luxation and is excessively rare at that. In our review of the literature we have collected 21 cases (including our own) which are presented in Table I. (Although we found references* to two more such accidents, we were unable to obtain the original articles.)

TABLE I

RÉSUMÉ OF 21 INSTANCES OF ARTERIAL INJURY RESULTING FROM DISLOCATIONS AT THE ELBOW

Case Reported by:	Compound Luxation	Vessel Involved	End-Result
1. Bourgeois [3]	Yes	A. Brachialis	Definite limitation of motion
2. M'Carthy [4]	Yes	A. Brachialis	Ankylosis
3. Holl [5]	Yes	A. Ulnaris	Ankylosis
4. Pirovano [6]	Yes	A. Brachialis	Almost complete restoration of function
5. Hofmokl [7]	Yes	Cubital Artery or Vein?	Definite limitation of motion at elbow
6. Parker [8]	Yes	A. Brachialis	Complete restoration of function
7. Bowlby [9]	Yes	A. Ulnaris	Slight limitation of extension
8. Molitor [10]	No	A. Brachialis	Gangrene and amputation
9. Monteggia*	Yes	A. Brachialis	Gangrene, amputation and death
10. Cruveilheir*	Yes	A. Brachialis	"Healing"
11. Hueter*	Yes	A. Brachialis	Amputation
12. Loehr*	Yes	A. Brachialis	Moderate return of function
13. Bell*	Yes	A. Ulnaris	"Healing"
14. Frera*	Yes	A. Brachialis	Ankylosis
15. Schrieber*	Yes	A. Brachialis	Good functional result
16. Jungst*	No	A. Brachialis (intima torn only)	Gangrene and amputation
17. Bolli [11]	Yes	A. Brachialis	Limitation of motion
18. Wulsten [12]	Yes	A. Radialis	Full restitution of function
19. Jeanneney and Vielle [13]	No	A. Brachialis	Volkmann's contracture, vicious cicatrix
20. Marnham [14]	No	A. Brachialis	Very slight limitation of extension
21. Eliason	No	A. Radialis and Ulnaris	Good functional result

* Quoted by Moliter.

In support of Cotton's statement we see from an analysis of Table I that 16 of the 21 cases were indeed examples of compound rather than simple dislocations. In 15 instances the brachial artery itself was the vessel ruptured. In five cases the tear occurred below the bifurcation, involving the ulnar artery alone three times, the radial once, and both vessels once. In Hofmokl's[7] case the vessel ruptured was thought at operation to be the brachial artery, but on microscopic examination it was adjudged to be a vein.

As in our case muscle injury often accompanied the vascular damage. In different combinations rupture of nearly every tendon or muscle anterior to the joint was reported by one author or another. Sharply contrasted to the frequency of accompanying muscle damage is the relative infrequency of injury to the median nerve. In 14 of the above cases we found definite statements as to the condition of the median nerve. In three of these it was re-

ported as ruptured. However, in only one instance (Holl's[5] case) was the rupture of the nerve actually confirmed anatomically. In the other two cases the tear was postulated on sensory changes which may have been due to tension or pressure on the nerve or to the vascular disturbance itself without actual rupture. At least in one instance these sensory changes cleared spontaneously. In one case the ulnar as well as the median nerve was torn.

Because of the vague manner in which the final outcome in some of these cases is reported, evaluation of end-results is rather difficult. However, with some reading between the lines we have compiled the following data. Four (19 per cent) of the 21 cases went on to gangrene and amputation with one death. Nine cases (43 per cent) showed definite loss of function even to a state of complete ankylosis in several instances. In the remaining eight cases (38 per cent) complete or nearly complete restoration of function was enjoyed.

Most of the cases of compound dislocation were treated conservatively. The bleeding was controlled, the dislocation reduced, and drainage plus antiseptic treatment instituted. In some cases repair of soft tissue damage was attempted. In a few instances bony resection was performed because of suppuration or in order to obtain reduction.

When we consider the cases of simple dislocation we see that two progressed to gangrene and three did not. On reviewing the treatment in these cases we find that in the three instances in which the arm was saved immediate incision with evacuation of the clot and reduction of swelling was practiced. In the other two cases operation was delayed for a period of days until gangrene was inevitable and amputation became a necessity.

On studying the collateral circulation at the elbow we see that it is a rich one and under ordinary circumstances should be adequate. The branches anastomosing in front of the medial epicondyle are: The anterior branch of the inferior ulnar collateral, the anterior ulnar recurrent, and the anterior branch of the superior ulnar collateral.

Those behind the medial epicondyle are: The inferior ulnar collateral, the posterior ulnar recurrent, and the posterior branch of the superior ulnar collateral.

The branches anastomosing in front of the lateral epicondyle are: The radial recurrent and the terminal branch of the profunda brachii.

Those behind the lateral epicondyle are: The inferior ulnar collateral, the interosseous recurrent, and the radial collateral branch of the profunda brachii.

There is also an arch of anastomosis above the olecranon formed by the interosseous recurrent joining with the inferior ulnar collateral and posterior ulnar recurrent.

When we consider, however, that the anterior anastomosing branches are probably ruptured along with the main vessels in this type of injury, it becomes doubly important to immediately combat any further reduction of blood supply to the forearm and hand. In subcutaneous rupture of the vessels with hemor-

rhage and swelling tending to compress the collateral branches, immediate incision with evacuation of the clot and control of hemorrhage is demanded.

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KLEBSIELLA PNEUMONIAE (*BACILLUS MUCOSUS CAPSULATUS*) BACTERIEMIA DUE TO PROSTATIC ABSCESS

REPORT OF A CASE WITH RECOVERY

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THE species of bacteria classified as *Klebsiella pneumoniae* (*Bacillus mucosus capsulatus* or Friedländer's bacillus) is a definite, though relatively unusual, pathogen. Prostatic abscess, while not uncommon, presents a well recognized clinical syndrome. By the laws of chance alone, therefore, one would expect them occasionally to coexist. Tenenbaum and Ravid,[1] however, appear to have been the only authors who have reported an instance of their concurrence, which resulted fatally.

Case Report.—A white male, age 48, was admitted to the Lankenau Hospital, November 2, 1936, complaining of fever and sweats for four weeks. His illness dated from the ingestion of some tainted oysters. The following day, he vomited the entire meal, subsequent to which he began to sweat profusely at night, running an evening temperature from 101° to 103° F., which became normal the following morning. He developed a greenish diarrhea consisting of from five to ten loose stools which persisted through the first week of his illness, after which time it was apparently controlled by a diet of hot milk. Two weeks before admission, he complained of burning on urination and noticed cloudy urine. A diagnosis of pyelitis was made and, on medication and forced fluids, the patient's dysuria was relieved and the cloudiness of the urine decreased.

Ten years before admission, he suffered from a corneal ulcer of the left eye which had broken down several times, the last occurrence having been eight months before

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admission. Roentgenologic examination of the sinuses, teeth and chest were negative. The tonsils had been removed and a fistula in ano had been incised. No prostatic studies were made at that time.

Seventeen months before admission, the patient had had his prostate examined by an urologist. The expressed secretion contained 80 pus cells per high power field. Shortly thereafter the fistula in ano developed and he was lost sight of until six months later, when another examination revealed 12 pus cells per high power field. No definite plan of prostatic therapy was instituted. The patient denied gonorrheal infection.

Physical Examination revealed a well developed, well nourished, middle aged man who appeared to have lost weight. Temperature 98.6° F.; pulse 100; respirations 20. A round opacity of the left cornea was present which measured 3 Mm. in diameter. Many teeth had been extracted, but those remaining appeared to be in good condition. Heart and lungs normal; blood pressure 108/58. Abdominal examination negative. No costovertebral tenderness or spasm was present. The genitalia were normal. The prostate was resilient, not tender, the left lobe slightly enlarged but no fluctuation was noted. Reflexes normal. R.B.C. 4,500,000; W.B.C. 20,000 with 81 per cent neutrophiles and 19 per cent lymphocytes; Hb. 86. The urine was acid, slightly cloudy and contained a few shreds. It showed 10 to 12 white cells per H.P.F. in a centrifuged specimen.

Course.—On the night of admission, a severe chill lasting one-half hour occurred. The temperature rose to 104.8° F. The next day the temperature was normal. The patient perspired profusely all day. This was followed in the evening by a similar second chill. Blood culture showed two colonies per cc. of the *Klebsiella pneumoniae*. No more chills occurred, but the patient continued to sweat profusely and developed a watery diarrhea. A culture of the feces also showed *Klebsiella pneumoniae*. Culture of the urine was also positive for the same organism. Investigations for typhoid, paratyphoid, malaria and undulant fever were negative. Cultures from the nose and throat showed *Streptococcus viridans* and *Staphylococcus albus* but no *Klebsiella pneumoniae*. The prostate was massaged and both smear and culture showed the *Klebsiella pneumoniae*. A subculture of these organisms was injected intraperitoneally into a guinea-pig. The animal died within 12 hours and the organism was recovered from its heart's blood and liver. Twelve hours after the prostatic massage, the patient experienced difficulty in voiding and within 36 hours developed retention of urine. The history, the slight enlargement of the prostate, the bacteriologic findings and finally the development of urinary retention after prostatic massage quite definitely established the diagnosis of prostatic abscess due to *Klebsiella pneumoniae*. On the following day, the ninth after admission, the patient was operated upon.

Operation.—Under spinal anesthesia, a perineal prostatotomy was performed and about 100 cc. of slimy, white pus were evacuated, which showed a pure culture of *Klebsiella pneumoniae*. A piece of rubber dam was placed in the prostatic bed and the wound was closed loosely about it.

Postoperative Course.—On the fourth postoperative day, a left epididymitis developed, followed, four days later, by involvement of the right epididymis which developed into an abscess. It was incised on the twenty-sixth postoperative day and slimy, white pus evacuated, which showed a pure culture of *Klebsiella pneumoniae*. The perineal incision gradually closed, the bilateral epididymitis eventually resolved, the urine became clear and the patient was discharged 37 days postoperative.

Discussion.—The case is interesting because of the unusual etiologic agent. As Tenenbaum and Ravid[1] pointed out, the *Klebsiella pneumoniae* is too frequently considered a respiratory pathogen. It does occur as the etiologic agent in a small percentage of cases of pneumonia.[2] Etienne[3] showed that it may infect almost every organ of the body. Cases of urinary

tract infection by the organism have been reported.[4, 5, 6, 7] It has also been cultured from the nasopharynx and gastro-intestinal tract of a small percentage of normal individuals.[2]

In addition to being interesting from a bacteriologic viewpoint, the case is instructive because it illustrated many features characteristic of prostatic abscess. Pelouze[8] emphasizes the importance of teeth, tonsils and prostate as a triad of focal infection in the male. He cites numerous cases of corneal ulcer with recovery after a concurrent prostatic infection was eliminated. According to Pelouze, prostatic infection in nongonorrheal cases is frequently a sequela of dental or tonsillar focal infection. Even if the primary foci are eradicated, the prostatic focus will maintain the systemic symptoms. He finds that 72 per cent of all men presenting symptoms of focal infection have infection of the prostate. In the case under discussion, focal prostatic infection probably contributed to the recurrence of the corneal ulcer.

Not only may chronic prostatitis be a metastatic manifestation of focal infection elsewhere, but prostatic abscess is often a metastatic manifestation of infection in other portions of the body. Bugbee[9] reported five cases of prostatic abscess following influenza. Sargent and Irwin[10] reported one case following an extensive furunculosis, another after dental surgery for chronic gingivitis, a third which occurred after an incision into an acute osteomyelitic abscess, and a fourth which coincided with the height of an attack of acute rheumatic fever. Kretschmer[11] had one case following a carbuncle. Kickham and Welch[12] and Randall[13] each report a case following one or more boils. None of these cases was gonorrheal. The fact has been repeatedly emphasized that although a certain percentage of prostatic abscesses follow gonorrhea, an appreciable number are certainly unassociated with venereal disease.

The marked systemic manifestations of fever, chills and sweats in the case reported are not only duplicated in the other instance of abscess due to *Klebsiella pneumoniae* infection, but in numerous other abscesses caused by streptococci and staphylococci. Kretschmer[11] noticed that 19 of his 43 cases of prostatic abscess had chills and high fever. When one remembers that the prostate is a compound racemose gland surrounded by unyielding fascial walls and is drained through very small ducts, the reason for severe systemic symptoms is apparent. Other symptoms noted by Kretschmer were frequency of urination, local or back pain, dysuria, retention of urine and those resulting from rectal pressure.

The treatment of prostatic abscess is perineal prostatotomy. Randall and Sargent and Irwin discuss this fully. The mortality by this approach is nil; the morbidity low; and the incidence of complications small. Epididymitis is the most frequent sequela but its incidence in a large series of cases is small. If the operation is performed properly, the occurrence of fistulae is negligible. Rupture of the abscess on a sound, perineal transurethral prostatotomy and drainage into the rectum are mentioned only to be condemned because of the increased morbidity and the frequency of fistulae

formation resulting from such procedures. The after-care should consist of prostatic massage until the strippings are free of pus.

CONCLUSIONS

(1) A second case of prostatic abscess due to *Klebsiella pneumoniae* is reported.

(2) The case illustrated the rôle of the prostate in focal infection as well as the striking symptoms which may accompany prostatic abscess.

(3) The treatment of prostatic abscess is perineal prostatotomy.

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CORRECTION

In the Annals of Surgery (**106**, 161, August, 1937) Jackson, Dickerson and Gunther reported their observations on cerebrospinal fluid pressure in cases of head injury following the intravenous injection of hypertonic sucrose solution. In the introduction to this article they referred to recent work by Parker and Lehman (Annals of Surgery, **104**, 492, October, 1936) dealing with the effect of blood and its constituents in the cerebrospinal fluid spaces in increasing cerebrospinal fluid pressure. Although a part of our conclusions was correctly stated, another and important part was apparently misinterpreted.

In their second paragraph they emphasize the "irritating" effects on the meninges of blood in the cerebrospinal fluid spaces and cite our results as illustrative of the assumption that such "irritation" is the cause of increased cerebrospinal fluid pressure. They say: "That the effusion of blood in the subarachnoid space is highly irritating, causing pia-arachnoiditis, has been known for years." Following a reference to Weed's work, they add: "Parker and Lehman, in experiments on dogs with lacerations of the brain, have found that the pressure of the cerebrospinal fluid varies directly with the amount of blood that escapes into the subarachnoid space. . . . The most irritating substance is the serum protein of the blood."

It is quite true that we found in experiments on dogs with lacerations of the brain that the pressure of the cerebrospinal fluid varies directly with the amount of blood that escapes into the subarachnoid space. However, we did *not* conclude that an increase of cerebrospinal fluid pressure results from an *irritating* effect of the protein of the serum. In our work, it was demonstrated that the serum is the least irritating fraction of the whole blood as judged by the degree of microscopic change in the meninges (Parker and Lehman, Table I). On the other hand, we observed that greater increases in cerebrospinal fluid pressure occurred following the replacement of measured quantities of fluid by equal quantities of blood serum than when the same quantities were replaced by whole blood or red blood cells suspended in normal saline solution (Parker and Lehman, Chart 11). From our data, therefore, we concluded that the increase in cerebrospinal fluid pressure resulting from the presence of whole blood in the spinal fluid is probably due to a corresponding increase of osmotic pressure of the cerebrospinal fluid from the serum protein present, rather than to the irritating effect of either the blood or its serum.

We feel that this correction is important. The literature of head injury is so confused at present that any further confusion should be avoided. We believe that the misinterpretation of our studies in the paper by Jackson, Dickerson and Gunther may lead students of the subject to a misinterpretation of our actual position.

Edwin P. Lehman
William H. Parker

REJOINDER TO CORRECTION

I quote the entire paragraph from my article, because if one reads the content, I believe there is no cause for any confusion.

"Not enough attention has been given to the withdrawal of blood from the subarachnoid spaces in cerebral injury. That the effusion of blood in the subarachnoid spaces is highly *irritating*, causing pia-arachnoiditis has been known for years. Recently Weed has shown that *blood serum* in the cerebrospinal fluid retards absorption of this fluid, causing it to collect in greater amounts in the subarachnoid system. Parker and Lehman, in experiments on dogs with lacerations of the brain, have found that the pressure of the cerebrospinal fluid varies directly with the amount of blood that escapes into the subarachnoid space and not with the amount of bleeding into the cerebrum or enlargement of the brain due to traumatic edema. The most irritating substance is the serum protein of the blood. It is this fluid constituent of the blood that can be withdrawn easily and safely by lumbar drainage of spinal fluid."

The sentence to which Drs. Lehman and Parker refer is: "The most irritating substance is the serum protein of the blood." The term irritating to which they take exception, is used here in the *clinical* sense and refers to the increase of cerebrospinal fluid, explained in the sentence following.

HARRY JACKSON

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